CONTENTS OF NUMBER 1, VOLUME 2

JULY, 1911

	PAGE
The Treatment of Sepsis in Scarlatina with Antistreptococcus Serum. Matthias Nicoll, M.D., New York	1
Accessory Sinus Suppuration in Scarlatina. Thomas Hubbard, M.D., Toledo, O.	11
Studies in the Metabolism of Atrophic Infants. Charles A. Pfaff, M.D., and Boudin S. Veeder, M.D., Philadelphia	19
A Preparatory Study of the Bacillus Acidophilus in Regard to Its Possible Therapeutic Use. Thomas Morgan Rotch, M.D., and Arthur I. Kendall, Ph.D., Boston	33
Anaphylaxis in Its Relation to Pediatrics. Godfrey R. Pisek, M.D., and Marshall C. Pease, M.D., New York	39
The Fundamental Requirements of an Infant's Nutrition. John Howland, M.D., St. Louis	56
Progress in Pediatrics	66

American Journal of Diseases of Children

VOL. 2 AUGUST, 1911 No. 2

THE OCCURRENCE OF INFANTILE PARALYSIS IN THE UNITED STATES AND CANADA IN 1910 *

ROBERT W. LOVETT, M.D.
BOSTON

The great prevalence of infantile paralysis in the United States in 1910 and its rapid increase in the last two or three years in this country, are matters which demand our serious consideration, and in the following paper will be presented the data obtainable on the subject, preceded by a brief résumé of the history of the disease in this country insofar as it bears on the present situation.

That infantile paralysis is not a new disease is a matter of common information, and it is of interest to note that the first probable allusion to it to be found in literature occurs in the book of Samuel, fourth chapter and fourth verse. It is as follows:

> "And Jonathan, Saul's son, had a son that was lame in his feet. He was five years old when the tidings came of Saul and Jonathan out of Jezreel, and his nurse took him up and it came to pass as she made haste to flee that he fell and became lame. And his name was Mephibosheth."

This short clinical history, although suggestive, is hardly convincing, but it is quite as likely to have been a case of infantile paralysis as are some of the cases reported as such in the year 1910.

The disease is first recorded as occurring in America in epidemic form in 1841 by Colmer,[1] as follows:

> "While on a visit to this parish, West Feliciana, Louisiana, in the fall of 1841, my attention was called to a child, 1 year old, slowly recovering from a hemiplegia. The parents, who were people of intelligence and unquestioned veracity, stated that either eight or ten cases of either hemiplegia or paraplegia had occurred during the preceding three or four months within a few miles of their home. Some of these recovered completely, others were improving. The little sufferers were all under 2 years of age and the cause seemed to be the same in all, viz., teething."

The account of this epidemic has, however, been questioned on the ground that it was only hearsay evidence and not substantiated, and the first authentic description of an epidemic of thirteen cases is credited to Bergenholz, a Swede, in 1881.

---

*Presented by invitation before the American Pediatric Society, Lake Mohonk, N. Y., June 1, 1911.

1. Am. Jour. Med. Sc., 1845, v, 248.

That infantile paralysis has existed in the United States for an indefinite time is perfectly familiar to us from the fact that we all know of adults affected whose history would reach back fifty years.

In 1875, Sinkler[2] reported that in the preceding four years he had seen eighty-six cases at the Infirmary for Nervous Diseases in Philadelphia.

The best evidence that I can find of the existence of infantile paralysis in our midst in any considerable degree for the last twenty-five years is derived from a study of the records of two hospitals, one in Boston and one in New York, which also contribute the best evidence that I have seen of the sudden increase of the disease in our midst in the last few years. The first named of these hospitals draws from a

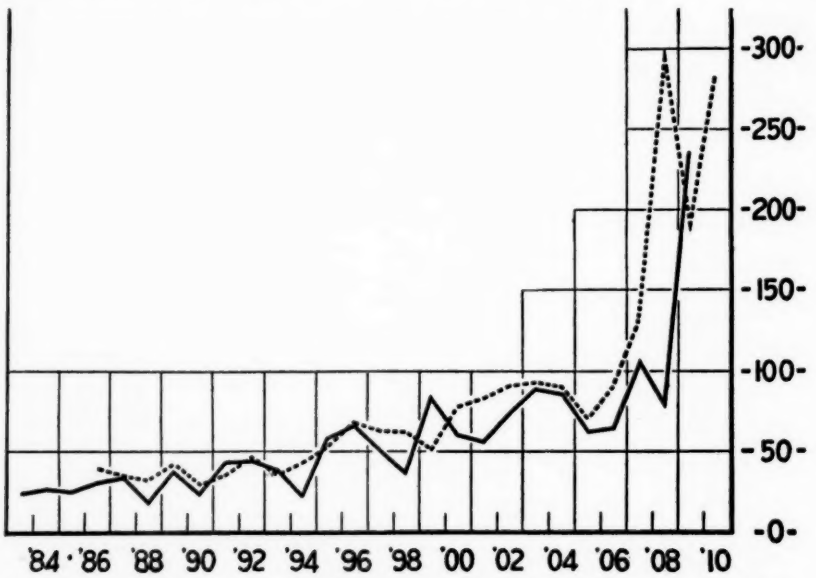

Chart 1.—Number of new patients with infantile paralysis treated at Children's Hospital, Boston, indicated by the solid black line; those treated at the New York Orthopedic Dispensary and Hospital by the dotted line; both by years.

large area and the clientele of both in the last twenty-five years has been more or less constant.

The accompanying chart (Chart 1) is constructed in part from the records of the orthopedic out-patient department of the Children's Hospital, Boston, and shows the number of new patients with infantile paralysis applying for treatment since 1883 in that department. The figures show that in 1883 we treated twenty-two patients, and that the number of cases with unimportant fluctuations rose steadily for twenty-five years,

2. Sinkler: Boston Med. and Surg. Jour., Nov. 23, 1893.

until 1909, when Boston was an epidemic center, when it rose suddenly to 235 cases.

The second institution analyzed on the chart is the New York Orthopedic Hospital and Dispensary, the figures of which were kindly furnished to me by Dr. Russell A. Hibbs, and which show in general the same facts. There were thirty-nine new cases in 1886, rising gradually to 1907, when a marked increase occurred. It will be noted that the New York increase began two years before that in Boston.

The first outbreak in the United States of the disease in any considerable degree was in 1894, when Caverly[3] of Rutland described an epidemic of 132 cases in the Otto Creek Valley, Vermont. In this epidemic Caverly attended to abortive cases, not under that name but as cases presenting the clinical symptoms without the paralysis.

In the same year was reported by Brackett[4] a group of ten cases in North Adams, Massachusetts. Both Rutland and North Adams are in railroad communication with Boston, and it is interesting to note that Putnam[5] in November of the previous year, 1893, had called attention to the increased prevalence of the disease in Boston in the preceding summer, the patients coming from different parts of the suburbs of Boston.

In the following eleven years, that is, from 1894 up to 1904, there were reported in the United States nine small epidemics (Chart 2), the second largest again in Massachusetts, consisting of thirty-eight cases,[6] and the largest, fifty-five cases,[7] in California, about San Francisco. The total epidemic cases reported in these eleven years, i. e., from 1894 to 1904, inclusive, in the United States were 157, or an average of about fifteen a year.

In 1905-6 no epidemics were reported.

In 1907 the most extensive epidemic ever known visited New York City and its surroundings and was estimated at 2,500 cases. In the same year were reported epidemics in Virginia (26 cases), Pennsylvania (100 cases), Massachusetts (234 cases), Michigan (20 cases), and Northern New York (29 cases); a total of about 2,900 cases.

In the year 1908 the disease was apparently quiescent, groups of cases being reported from Massachusetts (136), Michigan (30), Florida (16), Minnesota (60) and Wisconsin (60); a total of 302 cases.

In the year 1909 large epidemics occurred in Massachusetts, Minnesota, Kansas, Nebraska and Cuba, the total number of cases being 2,343.

3. Jour. Am. Med. Assn., 1896, xxvi, 1.
4. Brackett: Tr. Am. Orthop. Assn., xi, 132.
5. Putnam: Boston Med. and Surg. Jour., Nov. 23, 1893.
6. Painter: Boston Med. and Surg. Jour., cxlvii, 633.
7. Wood's Occidental Med. Jour., xvii, 77.

That infantile paralysis has existed in the United States for an indefinite time is perfectly familiar to us from the fact that we all know of adults affected whose history would reach back fifty years.

In 1875, Sinkler[2] reported that in the preceding four years he had seen eighty-six cases at the Infirmary for Nervous Diseases in Philadelphia.

The best evidence that I can find of the existence of infantile paralysis in our midst in any considerable degree for the last twenty-five years is derived from a study of the records of two hospitals, one in Boston and one in New York, which also contribute the best evidence that I have seen of the sudden increase of the disease in our midst in the last few years. The first named of these hospitals draws from a

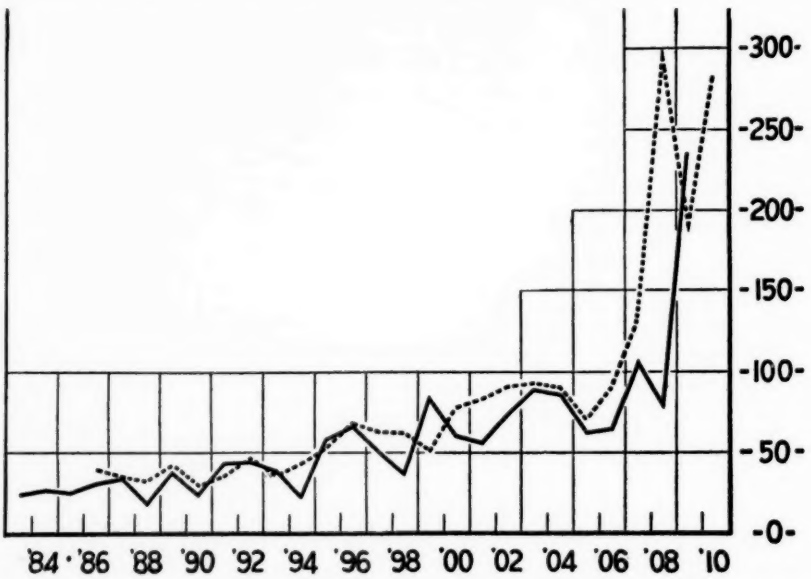

Chart 1.—Number of new patients with infantile paralysis treated at Children's Hospital, Boston, indicated by the solid black line; those treated at the New York Orthopedic Dispensary and Hospital by the dotted line; both by years.

large area and the clientele of both in the last twenty-five years has been more or less constant.

The accompanying chart (Chart 1) is constructed in part from the records of the orthopedic out-patient department of the Children's Hospital, Boston, and shows the number of new patients with infantile paralysis applying for treatment since 1883 in that department. The figures show that in 1883 we treated twenty-two patients, and that the number of cases with unimportant fluctuations rose steadily for twenty-five years,

2. Sinkler: Boston Med. and Surg. Jour., Nov. 23, 1893.

until 1909, when Boston was an epidemic center, when it rose suddenly to 235 cases.

The second institution analyzed on the chart is the New York Orthopedic Hospital and Dispensary, the figures of which were kindly furnished to me by Dr. Russell A. Hibbs, and which show in general the same facts. There were thirty-nine new cases in 1886, rising gradually to 1907, when a marked increase occurred. It will be noted that the New York increase began two years before that in Boston.

The first outbreak in the United States of the disease in any considerable degree was in 1894, when Caverly[3] of Rutland described an epidemic of 132 cases in the Otto Creek Valley, Vermont. In this epidemic Caverly attended to abortive cases, not under that name but as cases presenting the clinical symptoms without the paralysis.

In the same year was reported by Brackett[4] a group of ten cases in North Adams, Massachusetts. Both Rutland and North Adams are in railroad communication with Boston, and it is interesting to note that Putnam[5] in November of the previous year, 1893, had called attention to the increased prevalence of the disease in Boston in the preceding summer, the patients coming from different parts of the suburbs of Boston.

In the following eleven years, that is, from 1894 up to 1904, there were reported in the United States nine small epidemics (Chart 2), the second largest again in Massachusetts, consisting of thirty-eight cases,[6] and the largest, fifty-five cases,[7] in California, about San Francisco. The total epidemic cases reported in these eleven years, i. e., from 1894 to 1904, inclusive, in the United States were 157, or an average of about fifteen a year.

In 1905-6 no epidemics were reported.

In 1907 the most extensive epidemic ever known visited New York City and its surroundings and was estimated at 2,500 cases. In the same year were reported epidemics in Virginia (26 cases), Pennsylvania (100 cases), Massachusetts (234 cases), Michigan (20 cases), and Northern New York (29 cases); a total of about 2,900 cases.

In the year 1908 the disease was apparently quiescent, groups of cases being reported from Massachusetts (136), Michigan (30), Florida (16), Minnesota (60) and Wisconsin (60); a total of 302 cases.

In the year 1909 large epidemics occurred in Massachusetts, Minnesota, Kansas, Nebraska and Cuba, the total number of cases being 2,343.

3. Jour. Am. Med. Assn., 1896, xxvi, 1.
4. Brackett: Tr. Am. Orthop. Assn., xi, 132.
5. Putnam: Boston Med. and Surg. Jour., Nov. 23, 1893.
6. Painter: Boston Med. and Surg. Jour., cxlvii, 633.
7. Wood's Occidental Med. Jour., xvii, 77.

When we come to the analysis of the figures for 1910 we must remember that they were brought out by a systematic and extended inquiry undertaken by the Massachusetts State Board of Health, and probably had such an inquiry been possible in one of the earlier years a larger number of cases would have been discovered than now stand as reported in those years. Still, one cannot conceal the fact that in 1910 there apparently occurred a very much larger number of cases than before all over the United States, and that the extent and distribution of the disease in this country in 1910 was of a different character from that of any previous year.

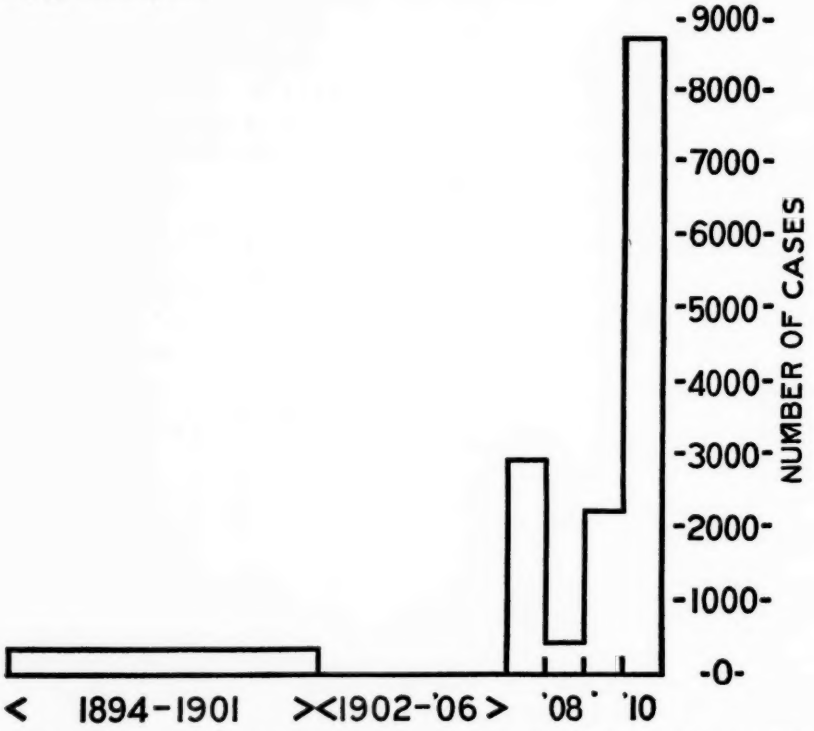

Chart 2.—Prevalence of infantile paralysis in the United States, 1894 to 1910.

There were about 8,700 cases reported in the United States in 1910, and if we contrast that figure with the years prior to 1904 when the average yearly number was fifteen cases per year we may appreciate what an enormous increase has occurred.

To summarize for a moment our facts so far collected: The disease has unquestionably existed in this country for many years. In 1893 the first reported tendency to increase is said to have showed itself in Boston, followed by the Vermont epidemic in 1894, and in the next eleven years by other small epidemics in various parts of the country.

Then came a period of quiescence followed by a violent outbreak in New York in 1907, since which, on the whole the extension of the disease has been rapid and in all directions. We are evidently now facing conditions favorable to the spread of the disease which did not exist in former years, and conditions which do not exist in Europe now, and it is for the purpose of bringing out this very point that I have thus dwelt on the earlier history of the disease in this country.

In Europe, although there has been an undoubted tendency of the disease to spread since 1905, when the great Scandinavian epidemic occurred, five-sevenths of 8,000 cases reported from all over the world for the five years ending in 1909 occurred in this country. The rela-

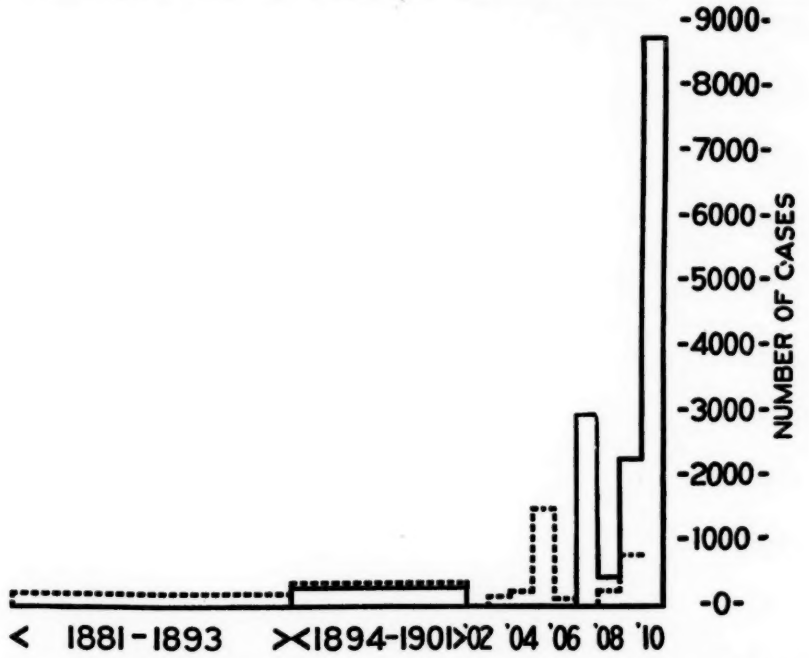

Chart 3.—Relative prevalence of infantile paralysis in the United States and Europe and Australia; the solid black line refers to the United States; the dotted line to the following countries: Italy, Sweden, Norway, Germany, Austria, France, England and Australia.

tive prevalence of the disease on the two continents is shown in the chart (Chart 3) and needs no comment. The disease is a reportable one in Sweden, Norway, Germany and Austria, so that in these countries, in any event, epidemics are not likely to fail to be reported.

The data with regard to the disease in the United States in 1910 were collected as follows: Dr. M. W. Richardson, the secretary of the Massachusetts State Board of Health, sent out several hundred letters of inquiry to state boards of health, to officers of state medical societies

DISTRIBUTION OF
INFANTILE PARALYSIS
IN UNITED STATES
IN 1910
LEGEND
DISEASE REPORTABLE BY LAW. NOT REPORTABLE IN OTHER STATES.
(F) - FROM A SERIES BY FROST
(EST.) - NUMBER OF CASES ESTIMATED
± - APPROXIMATE.
HAWAII 33
CANAL ZONE 1 (WHITE)
PORTO RICO ABSENT
BRITISH COLUMBIA 75
ALBERTA 11
WASHINGTON 300
OREGON 112
CALIFORNIA 100
NEVADA 9 (09-10)
IDAHO 96(F)
MONTANA 170 (EST.)
WYOMING RARE
UTAH 120(EST.)
COLORADO 9 (F)
ARIZONA 30 (EST.)
NEW MEXICO NONE KNOWN
NORTH DAKOTA 150
SOUTH DAKOTA 86
NEBRASKA 50
KANSAS 198
OKLAHOMA 20
INDIAN TERR.
TEXAS FEW
MINNESOTA 1000
IOWA 651
MISSOURI 174
ARKANSAS NO. INF.
LOUISIANA 50±
WISCONSIN 370 (EST.)
ILLINOIS 137 (F)
MICHIGAN 43
MISSISSIPPI RARE
ONTARIO 179
QUEBEC PRESENT
INDIANA 500 (EST.)
OHIO 52(F)
KENTUCKY FEW
TENNESSEE NONE KNOWN
ALABAMA FEW
GEORGIA FEW
FLORIDA 19
NEWFOUNDLAND 1
P.E. ISLAND NONE KNOWN
NEW BRUNS. FEW
NOVA SCOTIA PRES.
MAINE PRES.
NEW YORK 225
PENNSYLVANIA 1000+
WEST VIRGINIA 500
VIRGINIA RARE 350
N. CAROLINA FEW
S. CAROLINA 85(F)
MASS. 210 (EST.)
CONN. 48
R.I. 231(F)
168
70(09-10)
DEL. 8
MD. 300(EST.)
D.C.

Chart 4

and to prominent physicians in various parts of this country, its dependencies, and Canada. From their replies to those letters the data given in Table 1 have been compiled. In a few instances the figures have been taken from the Marine Hospital Service tables prepared by Frost, and such are marked (F). In certain instances where no reliable number of cases or no number at all was given in a state, and the number of deaths from infantile paralysis during 1910 was given, the number of deaths has been multiplied by ten, a conservative mortality per cent., and the number of probable cases thus estimated. In such cases the figures have been followed by the abbreviation (Est.).

TABLE 1.—DISTRIBUTION OF INFANTILE PARALYSIS IN THE UNITED STATES, 1910

Alabama*	Few	North Carolina	Few
Arizona	30 Est.	North Dakota*	150
Arkansas	No information	Ohio*	52 F.
California	100	Oklahoma*	20
Colorado	9 F.	Oregon*	112
Connecicut	168	Pennsylvania*	1000+
Delaware	8	South Carolina*	85 F.
District of Columbia	500	Rhode Island	231 F
Florida	19	South Dakota*	86
Georgia	Few	Tennessee*	None known
Idaho*	96 F.	Texas	Few
Illinois	137 F.	Utah*	120 Est.
Indiana*	500 Est.	Vermont*	48
Iowa	651	Virginia*	350
Kansas*	198	Washington*	300
Kentucky	Few	West Virginia	Rare
Louisiana	50 Approx.	Wisconsin*	370 Est.
Maine*	Present	Wyoming*	Rare
Maryland	300 Est.		
Massachusetts*	845	Hawaii*	33
Michigan	43	Porto Rico	Absent
Minnesota*	1000	Alberta	11
Mississippi	Rare	Canal Zone	1 White
Missouri	174	Philippines	None
Montana	170 Est	Newfoundland	1
Nebraska*	50	Nova Scotia	Present
Nevada	9 (1909-10)	Ontario*	179
New Hampshire	210 Est.	Prince Edward Islands	None known
New Jersey*	70 (1909-10)	Quebec	Present
New Mexico	None known	British Columbia*	75
New York*	225	New Brunswick	Few

*Disease reportable by law. (In states not starred disease is not reportable by law.)

Est.—No of cases estimated.

F.—From series by Frost.

Approx.—Approximate.

Mortality per cents. have not been allowed any importance in this tabulation, as they are only of value or significance in instances in which an epidemic has been carefully enough studied to bring out the total number of cases occurring. For example, one state in which the disease is not reportable, reports thirty-five cases and thirty deaths, which probably does not mean that the mortality was enormously high in that state, but that the deaths were reported and the non-fatal cases were not.

Although somewhat lower than the figures in foreign countries, there is reason to believe that the Massachusetts figures of 8 per cent. are approximately correct for that state at least, although the mortality per cent. in the District of Columbia in 1910 was only about 3 per cent.[8]

The map of the United States (Chart 4), on which has been marked the number of cases in each state for 1910, shows a total of about 8,700 cases, not counting Canada or such dependencies as Hawaii, and making no account of states reporting "a few," etc. In practically all cases not otherwise designated, the number of cases given is the number officially given out. Various terms have been used in the cases of states from which exact information was not obtainable, the term being chosen according to the information which was sent in.

The disease is now reportable by law in twenty-three states, which are shown shaded on the map, and various other states have the matter under consideration or may have legislated very recently.

A study of this map shows in the first place a wide-spread and general distribution of the disease with, in general, a focal occurrence and radiation from these foci. There is in general a scarcity of cases in the southeastern section of the country. In the New England states there occurred a group of cases, the largest number being in Massachusetts and Rhode Island. It is probable that the large number credited to Massachusetts is in a measure due to the careful investigation of the disease carried on there now for four years, as a result of which the medical profession is on the alert to report cases, so that the apparent prevalence there is probably exaggerated in comparison with other states.

An epidemic focus of considerable size existed in Pennsylvania, Maryland, North Carolina and Virginia, the latter state being the southern limit of any considerable extension in the East.

In the Middle West there was a large epidemic focus in Minnesota, Wisconsin and Iowa, some 2,000 cases being reported from these states, and in a circle around these three seriously infected states there existed in neighboring states from fifty to 200 cases per state, with over 500 cases in Indiana. An area of comparative immunity from north to south covered the Rocky Mountain region, but on the Pacific Coast there existed in Washington an epidemic center of 300 cases, with extension south to California and general involvement of the Southwestern states.

In Canada the disease appeared most extensively in the Province of Ontario, with 179 cases, with seventy-five in British Columbia and eleven in Alberta. New Brunswick reported a few cases, but no deaths, and there were cases in Quebec and Nova Scotia, with one in Newfoundland, but Prince Edward Island reported the disease as unknown there in 1910.

8. Washington Med. Ann., May., 1911.

The disease is reportable by law in Ontario and British Columbia and not in the other provinces.

As to our Southern dependencies, there were no cases in Porto Rico or the Philippines; one in a white laborer in the Canal Zone, and an epidemic of thirty-three cases in Hawaii.

It is disquieting to note that in April of this year (1911) an epidemic of twenty or more cases occurred in Louisiana,[9] which was so threatening that the governor was appealed to for aid in suppressing the epidemic. In Massachusetts in the four years during which the disease has been under observation it has occurred earlier each year, reaching its height in September in 1907, August and September in 1908, in August in 1909 and in July in 1910. It will be of importance to note whether this is a mere coincidence or whether the disease is really tending to occur earlier as it spreads.

Such are the data that it has been possible to bring to light, but it is of course evident that the number of cases thus officially reported is a poor criterion by which to judge the total number that have occurred. In half of the states the disease is not reportable and it is naturally impossible to obtain any reliable information from these, and where it is reportable many cases are either unrecognized or unreported when recognized. The disease is so dreaded by the public that there will be a tendency to the suppression of information, especially in summer resorts.

In view of these facts, it may seem to this society worth while to take action to urge again on all state boards of health the importance of placing this disease on the list of those reportable by law. Several states in which the disease is not now reportable have the matter under consideration and the situation is too serious not to warrant every effort to place the disease where it may be studied and watched.

Several state boards have set on foot investigations as to the prevalence and distribution of the disease and have formulated blanks for distribution. But desirable as this is, we need more than this. The important questions that we want to have answered, the facts that will help us in finding out more about the disease, are not to be settled by the routine investigation of epidemics.

These are to be found in literature by the dozen, and anyone familiar with the subject can tell you in advance just what such an investigation will show. The disease will be found in scattered foci, with cases radiating from these foci. It will reach its height in the late summer; it will follow the lines of travel; it will affect mostly children in the first dentition; the mortality rate will be from 3 to 15 per cent. In October the epidemic will begin to die out. Data of this class exist in abun-

9. New Orleans Times Democrat, April 27, 1911.

dance and are useful only in giving us the distribution of the disease in a given locality.

What we do need is a careful house-to-house study, made, if possible, during the epidemic by competent medical men on salary, giving their whole time to the work. These men should examine most carefully the premises, the neighborhood, and every detail of the patient's life, environment and habits, his points of contact with other cases, with sick animals, the history of wounds and insect bites, his food, antecedent illnesses, etc.

The solution of the mystery of this disease may come from the laboratory or from the field work, or from both, but field work to be of any use must be intensive. The collection of routine data will not settle the question of etiology.

Such a plan as this means financial support, and in Massachusetts we have found the legislature ready to give us such support, and not only the legislature, but the public, a voluntary subscription of $5,000 from private sources having been placed at the disposal of an expert for the study of animal diseases akin to infantile paralysis. In addition to this the Massachusetts legislature of this year has appropriated $10,000 for the use of the State Board of Health in the coming year in the study of the disease. These facts show how a community feels where the disease has prevailed extensively.

Finally, it would be of value if some bureau or central committee for the interchange of information could be established with regard to the disease in America and the provinces. Such data as are presented above are only secured now by the expenditure of much effort and a considerable amount of work and money. If the disease is to increase in the near future at the same rate as in the last two years in America, it is important for the medical profession to have at its disposal every facility for obtaining information and every opportunity for study of the disease that is possible. On the one side we run the risk of alarming the community by the publication of such facts as these, but on the other hand, if we neglect to look at the situation as its exists, we run the risk of being charged later with having underestimated the seriousness of the present situation.

234 Marlboro Street.

THE CEREBRAL FORMS OF POLIOMYELITIS *

HENRY KOPLIK, M.D.
NEW YORK

During the first epidemic of poliomyelitis and in the recurrent outbreaks in New York and vicinity there have occurred here and there a number of cases which have been of great interest because of their close simulation of certain cerebral conditions which I shall mention later. I refer to those cases of poliomyelitis which belong more particularly to the cerebral group of this affection. Polioencephalitis or encephalitis, as it is called, was first brought into closer relationship with poliomyelitis by Medin. In the large Swedish epidemic of 1905 there were many of these cases, and Medin in his early writings insisted on the general identity of this set of cases with poliomyelitis as it was then known. His assumptions were at first disputed by men of no less genius than Henoch, who thought that Medin in describing the cerebral forms of poliomyelitis as identical with the spinal forms in etiology and pathology had rather committed an error of clinical observation and mistaken his cases for something of another character. How certain and true the original observations of Medin have been time has shown, and Harbitz and Scheele have proven beyond question that the infectious agent producing epidemic poliomyelitis may extend to any part of the cerebrospinal system, and may affect both the gray and white matter of the brain and cord. Moreover, there is in all cases of poliomyelitis a real meningitis; that is, the processes of infection expend themselves on the membranes of the brain and cord. There is an inflammation and infiltration of these structures, and from the vessels of the pia the toxic or infectious agent enters the tissues of the brain and cord, there effecting changes of greater or lesser severity. Thus the consequent symptoms will differ in sets of cases according to the localization of the inflammatory processes at play.

The cases to which I especially desire to call attention are those in which the structures of the brain, medulla and pons are affected, leaving the cord for the most part unaffected permanently. These cases have been previously described by various writers as encephalitis or polioencephalitis superior or inferior of Wernicke or of poliomyeloencephalitis of Strümpel. We may group all these descriptive clinical pictures under the entity of polioencephalitis. This would also include the pontine forms of encephalitis of Oppenheim. The general picture

*Read before the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

of polioencephalitis is cerebral, the symptoms are cerebral symptoms with, in certain cases, added palsies. Thus if the nuclei of the oculomotor nerves are affected we have with the cerebral symptoms an ophthalmoplegia of greater or lesser extent, identical with that which Wernicke describes as polioencephalitis superior. If the nuclei of the facial nerves are affected and the gray matter in the floor of the fourth ventricle, the cerebral symptoms are supplemented by facial palsies, and thus there is produced the picture described by Wernicke as polioencephalitis inferior. If the process extend still further down it may involve the nuclear masses of the hypoglossus and more vital nuclei, and then symptoms of paralysis identical with acute bulbar paralysis are produced. Certain it is that the forms of polioencephalitis will merge into one another. Thus, cases occur in which there are isolated palsies, such as those of the muscles, of one or other of the eyes; and then cases occur in which eye and facial nuclei (muscles) are involved, and others in which all these are affected and bulbar symptoms occur. The last group rather number the fatal cases, though I have seen a number of bulbar cases in which recovery occurred.

The cases which are limited in their extent of involvement of the ocular and facial nuclei, and which are accompanied by cerebral symptoms, are those which to me have been of greatest interest, because in such cases of polioencephalitis I have had the greatest difficulty, in the face of the cerebral symptoms, accompanied, as they were after a while, with nuclear palsies, to differentiate them from forms of meningitis either of the acute suppurative (meningococcic) variety, or the tuberculous forms of the disease. In fact, in some cases the clinical similarity of forms of polioencephalitis with forms of meningitis is so close that it is only by careful observation that we can differentiate the two, and then only with a possibility of some doubt. In order to facilitate clinical study of polioencephalitis it will be best to first draft in outline the general history of these cases.

A child in previously good health, without any marked prodromal symptoms, develops fever which may be quite high or may be moderate in degree. There may be complaint of some headache, there may be vomiting. Such a child will continue for twenty-four hours to be up and about, and after the initial period it is noted that the fever continues as does also the headache, and after a time the patient is too sick to be about, complains of a tired feeling and goes to bed. It is then noted that the sopor deepens, and then the temperature may subside to the normal or continue a little above the normal. In some cases from this time on the history is that the patient is at times delirious, irrational, complains of headache, and resents being disturbed. There is extreme hyperesthesia. Some patients complain of pain in the nape

of the neck; there is marked rigidity with the Kernig sign in the lower extremities, and signs of a mild hydrocephalus (Macewen). Such patients may have a maudlin delirium, lie crouched in bed and refuse to take food. Close examination may discover isolated ocular palsy in some cases, and this is the only objective palsy present. In other cases with palsy of some of the ocular muscles there is slight facial palsy of one or the other side, and in still other cases these palsies may be combined with a very mild weakness of one or the other upper extremity. After a week or two, the patient gradually becomes more rational, the sensorium is brighter and he begins to recognize objects and talk rationally. If during the illness the patient is caused to stand, there is noticed a very marked ataxia and vertigo, with Romberg's symptom. As convalescence is established, the ataxia is the last symptom to improve. The hydrocephalus may persist, the compromised mental capacities may not return to the absolute normal as soon as one would expect. The temperature has during the illness, directly following the period of invasion, been normal, or, in exceptional cases, there may have been a rise of 2 or 3 degrees, with a fall to the normal daily for a week or more. As the patients convalesce they are able to sit up, this not having been hitherto possible. Speech is more distinct, due to the recession of the ataxia.

This is a sketch of the common picture. When recovery is established there may remain a strabismus, or a very mild form of ataxia in the gait, an uncertainty as it were. In one or two of my cases I have seen optic neuritis, such as choked disk, in the course of the disease, and this also may retrograde, the eyesight being entirely restored. In other cases, the eyesight which has failed during the illness may progress to absolute blindness, and this in turn may slightly improve, as in one of my cases, so that after a lapse of months the eyesight may have improved from absolute blindness to the ability to distinguish gross, large objects. In another group I have seen a complete unilateral ophthalmoplegia with dilatation of the pupil of the affected eye.

I have related enough of the symptomatology of this form of encephalitis or polioencephalitis to show how close the similarity to a cerebrospinal meningitis may be, the sudden onset, the high fever, the rigidity of the neck, the headache, the Kernig, all run close to the symptom-complex of a meningitis, and yet close study will show some differences. There is in polioencephalitis a short preliminary period in which the patient, having had a high fever, continues to be about. There is also an increasing sopor which extends over days; this is quite unlike the onset of a cerebrospinal meningitis. In these two points we can sometimes differentiate between the two diseases. Here, however, the dissimilarity ceases. In a recent outbreak of polioencephalitis in Staten

Island these two points stood out quite sharply on the clinical canvas, namely, the period of a day or so of high fever in which the patients did not quite take to bed, and then the period of fever and increasing sopor with the addition of all the symptoms of true meningitis.

Another set of cases of polioencephalitis are still more perplexing, inasmuch as they closely simulate another type of meningitis, the tuberculous form. A patient having been in previous good health will develop fever with some vomiting; the fever may be low, 102 or 103 F., or high, 104 to 105 F. The fever continues for a day or more and then sopor sets in, the temperature drops to the normal, the patient becomes completely unconscious. With this unconsciousness there is marked hydrocephalus, facial palsy, ocular palsy, such as strabismus, with loss of reflex at the knee, no Kernig, and a Babinski reflex. There may be a *tâche cérébrale*. After five or seven days of illness, the picture is the exact counterpart of a tuberculous case. The patient lies absolutely flaccid; there may be but very mild rigidity of the neck, there is Cheyne-Stokes respiration, and absence of reaction to mechanical stimuli in the presence of a normal or slightly raised temperature. After a few days the patient may succumb, but in many cases may come out of the coma and regain consciousness and power in the extremities. Such cases I have seen.

In another form the patient may have had a very short period of fever, which may have come on suddenly. Then after a few days the temperature falls to the normal, but the patient is noted to be stupid, and to act as if in a trance; there is mild hydrocephalus, but the sopor is the principal symptom. A bright child is noticed to act stupidly; begs to be left alone. There is hyperesthesia. All of these are present in face of a normal temperature. Gradually the patient after two or three weeks becomes brighter, takes an interest in surroundings, and the ataxia, which in some cases amounts to absolute inability to walk, in others to staggering gait with vertigo, gradually improves. The similarity of these cases to tuberculous meningitis is exceedingly close. There is one very salient point of difference. In cases of polioencephalitis the onset is sudden. It is especially noticeable that the children have previously been in excellent health, when they are attacked by the disease within twenty-four or forty-eight hours at the most. In this respect the two maladies are far apart. In tuberculous meningitis the onset is gradual, and cases of sudden onset are extremely rare; in fact, I have not seen an authentic case in several hundreds of cases. In tuberculous meningitis there is a state of sopor in which some preservation of intelligence and of the surroundings exists, which does not last long, but will deepen into coma; whereas in polioencephalitis there is a diminution of the sopor, and finally after a week or two the patient is observed to be brighter.

CASE REPORTS

CASE 1.—L. D., male, aged 5 years, has had rachitis. Three years ago he had scarlet fever and diphtheria. The tonsils had been removed.

Family History.—This was negative.

Personal History.—Five weeks before admission to the hospital the patient was taken with high fever, headache and prostration. The fever apathy continued for two weeks, during which time the child vomited frequently. The fever then ran a lower course and the child became somewhat brighter, complained of severe headache, vomited occasionally, and was constipated. The patient complained of pain in the right eye and right hand. There had been no convulsions. The child was quiet but the parents thought it did not sleep. There was sighing respiration.

Examination.—When admitted to the hospital: The patient was soporose, although he answered questions. There was slight rigidity of the neck, and a tendency to yawn. There was some hydrocephalus on the right side. The reflexes were exaggerated; the pulse equal, regular, no paralyses noted of any kind. There was slight neck rigidity, *tâche cérébrale*, signs of hydrocephalus on both sides; later on the abdomen was retracted; *left internal strabismus*, patient stuporous but conscious when roused; no evident paralyses. A lumbar puncture yielded 30 c.c. of clear fluid under some pressure. A day subsequent to admission the patient was brighter. An examination of the fundus oculi revealed some small retinal hemorrhages suggesting compression of the cerebral retinal arteries but no choked disk.

Five days after admission patient was conscious with the above ocular palsy, but interested in his surroundings; some exaggeration of the knee-jerk. On walking the patient showed some tremors; complained of headache, was apathetic, pupils uneven, right larger than the left. Four days subsequently he was still apathetic and complained of headache.

A second lumbar puncture four days after the above entry yielded 40 c.c. of clear fluid under some pressure.

Two weeks after admission the patient was still apathetic, soporose, with neck rigidity, and showed slight flatness of the right side of the face.

The eyes examined by Dr. May at this time showed optic nerve atrophy, so-called postneuritic atrophy, with hemorrhage in the retina. The patient was brighter but there was still some neck rigidity and signs of hydrocephalus.

After four weeks the patient was able to be out of bed; there was some mental obtuseness, marked signs of hydrocephalus; no blindness. There was a distinct ataxia or cerebellar gait; mentality continued below the normal. The patient was up and about, without temperature and played with other children.

Puncture fluid examined showed no bacteria; 100 per cent. lymphocytes; some reaction for sugar and albumin.

The von Pirquet tuberculin reaction was negative; blood showed 12,000 leukocytes, with a differential count of 51 per cent. polynuclears on admission. On discharge, or near that, the count was 8,000 leukocytes.

The temperature was normal after the first twenty-four hours' stay in the hospital, with the exception of a rise in temperature, due to an injection of the serum of Flexner as a safeguard, should examination of the fluid show meningococci.

Discussion.—This is a typical case of polioencephalitis resembling very much a tuberculous form of meningitis—the slight rigidity, stupor, hydrocephalus and low leukocyte count. The history, however, showed an acute onset five weeks before admission to the hospital. The puncture fluid also showed fully 100 per cent. of lymphocytes, a fact which might very well be linked with tuberculosis. The child was discharged from

the hospital well, however, with the remains of the encephalitis in the form of hydrocephalus and impaired mentality. The only paralysis during the illness was ocular.

CASE 2.—J. C., male, aged 7½, was admitted Dec. 22, 1908.

Family History.—Negative; no tuberculosis.

Past History.—None of the exanthemata; was perfectly healthy before the present illness; no pulmonary symptoms; bowels always normal; no urinary symptoms.

Present History.—For the previous two weeks the parents had noticed that the child had not acted as he did previously; he would cry out suddenly and then laugh; was pale; had no fever; no other symptoms until three days prior to admission when he suddenly became stuporous, cried out, complained of headache. Since then the stupor had deepened, the child almost constantly moaning and crying; no convulsions.

He had slight fever, no retraction of head, no photophobia; neck was somewhat stiff; no vomiting; bowels had been obstinately constipated; did not take any nourishment; no twisting of the face, and the child did not move its right arm as well as its left; occasionally cried out at night; with grinding of the teeth.

Physical Examination.—Fairly well nourished, lay in a stuporous condition; head somewhat retracted, patient constantly sighed and moaned with grinding of his teeth; restlessness during examination; seemed unable to move the left arm and leg, respiration was very irregular; practically no rigidity of the neck; some Macewen, especially on right side of the head; *tâche* present; no Kernig, no hyperesthesia, slight photophobia. Mucous membranes normal; no ataxia; no herpes; ears negative; eyes, both upper lids somewhat ptosed, pupils equal, regular, reacted to light; eyes had a slight nystagmus-like motion; no strabismus; conjunctivæ somewhat injected; no petechia; some excoriation about the alæ nasi; teeth and gums in fairly good condition; sordes on lips; tongue coated. Posterior cervical and a few small axillary glands enlarged. Examination otherwise negative; chest fairly well formed; lungs negative; heart normal; action somewhat irregular and rapid; no murmurs; abdomen retracted, lax, no pain; normal; liver normal; spleen negative.

Extremities: Right arm somewhat spastic, hand held clenched, and, as noted above, the child was inclined to move left extremity more than the right; knee-jerks exaggerated. No Babinski, no ankle-clonus.

December 23 lumbar puncture; 33 c.c. of clear fluid under moderate pressure removed; tuberculin cutaneous reaction negative. White blood cells 10,000; 64 per cent. polynuclears.

December 24. General condition somewhat better; less irritable, lay in a semistuporous condition; eyes slightly rotated to the left; no rigidity of neck; no Kernig. Second tuberculin reaction negative.

December 25. Examination of the eyes negative.

December 27. General condition fair; still irritable; did not speak; rigidity of the neck; no signs of hydrocephalus; pupils equal; knee-jerks exaggerated; left tendon reflexes exaggerated; physical condition the same.

December 28. Lumbar puncture; 20 c.c. of clear fluid removed.

January 1. The patient for the previous few days had had periods of stupor and maudlin delirium, in which he cried in a low tone; did not answer questions; did not seem conscious of his surroundings; no paralysis of the extremities, with the exception of the right upper extremity, which seemed to be weaker than its fellow; patient turned his head from side to side constantly; did not take nourishment; no signs of nuclear involvement in the shape of paresis or paralysis.

January 2. Tuberculin reaction negative; general condition much improved; very noisy and delirious most of the day; had a hot bath and then became

brighter; seemed to see and hear when spoken to, but did not speak; he motioned with his hands. Very noisy the previous night; took nourishment better; lungs and eyes negative; no paralysis; moved the left arm more than the right; knee-jerks exaggerated.

January 6. The patient in the morning was conscious; sat up in bed with a meaningless smile, when he talked speech was indistinct; had a nasal timbre. Patient did anything he was told to do; had marked loss of power in upper and lower extremities; had a Romberg; when he stood or walked he staggered; his arm and fingers taking on position of athetosis; had no paralysis or paresis of facial muscles; expression of eyes rather vacant, but was conscious and brighter.

January 9. Patient much quieter and brighter, had at times an idiotic smile; speech somewhat indistinct, and had a nasal tone; slight flatness of right side of face; tongue deviated slightly to the right; pupils central—reacted to light; right grip not as strong as left; no apparent atrophy, used arm fairly well; the right leg was quite as strong as the left; knee-jerks active; otherwise negative.

January 16. Discharged well; no paralysis; bright; speech still somewhat nasal.

The temperature the first week, from December 21 to 28, ranged from 98.5 to 99.8 in the rectum. After that it remained normal for four weeks, when he was discharged.

The urine was examined three times during the stay in the hospital and was found negative. The lumbar puncture fluid was examined twice.

January 2, Cytology, 100 per cent., lymphocytes; bacteriology, negative; traces of albumin. The second specimen 50 c.c.; report of sugar reduction; 95 per cent. lymphocytes; mononuclears; no bacteria. Pathologist thought it had more the character of a transudate than an exudate.

Discussion.—In this case there is an imperfect previous history in that no sudden onset with fever was obtained, but there was a period of two weeks of mental irregularities, slight fever and increasing sopor. The patient on admission to the hospital was unconscious and delirious. This delirium was of a distinctly maudlin variety and cleared up completely, leaving a bright intellect. There was on admission, also, rigidity of the neck, vomiting and headache. There was no real paralysis or strabismus. The reflexes were increased. There were signs of internal hydrocephalus. In this case there was a distinct marked leukocytosis, 30,000, with a polynuclear blood-count of 88 per cent. The puncture fluid also showed a lymphocytosis of 100 per cent. and 95 per cent., sterile to culture; some albumin and sugar. There was during the course of the affection slight flatness of one side of the face, some slight deviation of the tongue, and a nasal timbre to the voice. The latter persisted until his discharge.

CASE 3.—J. H., aged 4½, was admitted to the service March 2, 1909.

Family History.—No tuberculosis; the stepmother had a cough and hematemesis and saw the child frequently.

Previous History.—No measles, scarlet fever, pertussis or diphtheria; at the age of 6 months the patient had pneumonia for five days.

Present Illness.—This began five weeks prior to admission with occasional vomiting, which increased in frequency until the child vomited after each meal. No vomiting occurred in the previous two weeks. At that time the child complained of headache and pain in the abdomen, and continued to complain of

headache up to admission; had marked cough for a short time two weeks prior to admission and began to be drowsy and slept a good deal of the day; was conscious and recognized mother and asked for food, and played with her toys until five days prior to admission, when she developed rigidity of the neck. For the previous five days the child had seemed to be brighter and had remained in bed, up to that time she was up and about; *she did not seem to see well.* No fever or paralysis; the bowels were constipated; history of low temperature; no febrile movement.

Physical Examination (by house physician).—General condition poor, though fairly well nourished; marked rigidity of neck with Macewen; no Kernig; *tâche cérébrale* present; patient lay in a stuporous condition; could not be roused; made motions with the hands, did not talk; no hyperacusis, no photophobia; somewhat irritable when disturbed; no eruption on the skin; the ears were negative.

Eyes.—Left pupil larger than the right; they reacted to light; conjunctivæ negative; left internal strabismus; no facial paralysis; teeth and gums in fair condition; tongue coated, moist; throat slightly red; larynx, trachea, and thyroids negative; a few axillary glands could be felt; chest fairly well formed; otherwise negative; heart negative; abdomen negative; liver also; spleen not felt; genitals negative, with slight discharge; no edema of the extremities; knee-jerks exaggerated; there was ankle-clonus on both sides; there was a Babinski on left side; no paralyses.

Synopsis.—Stupor, irritability, rigidity, Macewen, *tâche*, ankle-clonus, Babinski, exaggerated knee-jerks, left internal strabismus.

March 3. Lumbar puncture; 30 c.c. of clear fluid containing flocculi was removed. Blood examination: Leukocytes, 30,000, polynuclears 88 per cent. Fundi of eyes examined; negative.

March 5. General condition about the same, patient was in bed; stuporous, but could be roused and then was irritable; moderate retraction of head, marked rigidity of neck, Macewen, slight Kernig; *tâche* present; slight weakness of the left external rectus; no paralysis nor paresis; did not void urine; must be catheterized. Respiration cerebral; no clonus, no Babinski.

March 7. Patient was irritable when disturbed; quiet when left alone; had a Kernig, rigidity of neck, Babinski, no Macewen; cries out. Lumbar puncture; 33 c.c. of clear fluid obtained; contained flocculi.

March 10. Patient was conscious; irritable and disposed to cry; sat up in bed when not watched; noticed everything around the bed. Slight Kernig with Babinski, especially on right side; rigidity of the neck; took nourishment; fundus of the eye normal.

March 12. This a. m. the patient was noisy; had distinct retraction of head; rigidity, Kernig, Babinski, opisthotonos; no paralysis of the facial muscles; took nourishment fairly well; was conscious; pulse slow and regular. White blood cells, 12,200; polynuclears 71 per cent.

March 14. Patient was more rational; sat up in bed; no paralysis; there was slight rigidity of neck, slight Kernig, no Macewen; chest and abdomen negative; took nourishment quite well; tuberculin reaction negative.

March 15. Improvement continued; patient sat up and noticed objects; was less irritable; had slight internal strabismus on the left side.

Patient's general condition was good; was more conscious; more or less aware of surroundings, no rigidity, no Kernig, slight Macewen on left side, no paralysis of limbs. Weakness of the left internal rectus.

March 17. Patient was examined with reference to paralysis; none of the face and extremities was found; strabismus still noted.

March 28. Patient had been up and about the last week; had only a left internal strasbismus left. Discharged.

During the patient's stay in the hospital the temperature ranged from 98 to 100.8 F. in the rectum during the first week, and then fell to normal; pulse and

respiration ranged from 20 to 30 for the latter to 90 to 136 for the former, the latter during the fever. When she was up and about the patient's pulse and respiration were 80 and 24 respectively.

The night nurse noted that during the first week the patient slept fairly well, but cried out at night and was restless at times; it was necessary to catheterize the patient; but after March 6 the patient, though restless, slept fairly well without any delirium. The urine examined during the patient's stay in hospital was negative.

The cerebrospinal fluid examined was negative on first puncture as to bacteria; there was a slight amount of albumin present and some sugar.

The second lumbar puncture, March 10, gave a cytology of mononuclears of 98 per cent., with no bacteria to culture or to spread; there was some albumin, 2 mg., and no sugar.

Discussion.—I saw this case in consultation. The onset was more or less acute. The subsequent history resembled a tuberculous meningitis, and the diagnosis was placed as a probable instance of this disease. In the hospital the symptoms cleared up, so that the patient, who was exceedingly bright, was up and about after two weeks. It is to be noted after discharge that though the patient's eyesight was good she returned in a month with a history of blindness of sudden onset. This, after a while, cleared up so that the patient could discern objects clearly. The fundus showed an optic atrophy. In the course of the affection there was a blood leukocytosis of 30,000, with a polynuclear count of 88 per cent. The fluids obtained by lumbar puncture gave a lymphocytic cytology of 98 per cent., some albumin, no sugar. The urine was negative; as also the lungs. Repeated von Pirquet skin tuberculin test was negative, and the temperature for the stay in the hospital did not exceed the normal after the first week. This case so closely resembled a tuberculous meningitis that a differential diagnosis without prolonged observation seemed impossible.

CASE 4.—S. F., schoolgirl, aged 11, was admitted to the hospital Feb. 8, 1909.

Family History.—Seven other children living and well. No history of tuberculosis.

Previous History.—Measles, no scarlet fever, no pertussis, no diphtheria, occasionally sore throat, no rheumatism, no pneumonia, no other complaint.

Ten days prior to admission the patient was taken ill and was in bed with high fever, vomiting, headache, malaise; then patient was up and about, but complained of occasional headache until February 7.

Present Illness.—The day before admission she had severe headache, and began to vomit; this continued until the day of admission, when she had general convulsions. Starting with a severe convulsion she had passed into a state of unconsciousness with some fever. The convulsions were repeated and back and neck became rigid; the bowels were constipated; there was no cough or vomiting on day of admission to hospital.

Physical Examination.—(By house physician.)—General condition fair; patient well nourished; slight soporose condition; patient continued to lie on the left side; conscious; irritable; there was some rigidity of the neck; marked Macewen; slight Kernig; *tâche cérébrale.* Patient could be roused from soporose condition; did not seem to be conscious, but simply moaned and cried; respiration somewhat irregular; cheeks flushed; put hands to head at times; twitching;

no retraction of the head. The skin showed some flea-bites, *"tâche bleuatre;"* no petechia; ears and mastoid negative; pupils regular; central, easily dilated; conjunctivæ injected; no paralysis; there was sordes in mouth; teeth and gums in good condition; tongue was coated and moist; throat showed muco-pus; no facial paralysis; thyroids and spine negative; few small axillary and inguinal glands to be felt; chest negative; somewhat sunken; abdomen retracted; liver, spleen and genitals negative. Extremities: Slight edema over the tibias; knee-jerks not obtained; no Babinski; no paralyses.

Synopsis.—Stupor, Macewen, Kernig, rigidity of the neck, *tâche cérébrale.*

February 9. Lumbar puncture; 35 c.c. of clear fluid removed under great pressure, and 30 c.c. of Flexner serum injected as a precaution should meningococcus be present on examination. White blood cells, 72,000; polynuclears, 79 per cent. Cutaneous tuberculin reaction negative.

February 10. Patient lay in a crouched position; was irritable when disturbed; cried out and was exceedingly hyperesthetic; retraction of head, rigidity, Kernig, as on the previous day; arms and extremities showed some edema still present; patient had ordinary redness of fauces; chest negative; patient did not take nourishment.

February 11. Patient had a general exanthematous rash (serum); patient lies in same position as on the previous day; general condition about the same; delirious when disturbed; rigidity and Kernig still present. Nurse reported that patient sat up and took notice of things.

February 12. The patient was much improved; opened her eyes and seemed to notice objects; was much clearer and did not resist quite so much. There was still very marked Kernig and very marked rigidity of the neck and retraction of head; there was also mydriasis when the head was flexed and slight strabismus on the left side.

February 13. When the patient was admitted the urine was of a distinctly brownish tint; it had now become clear but was distinctly colored; estimate of urine very difficult on account of the involuntary discharges; patient when left alone was very quiet; when interfered with still resisted; did not answer questions. Patient seemed to be more conscious, but was apparently deaf; no paralyses; Kernig still present.

White blood cells, 12,000; polynuclears, 83 per cent; fundus of the eyes normal.

February 14. Patient the previous night sat up; was quite logical, but apparently deaf; when any one came near her the patient was frightened, but was more rational than the previous day; no edema of the tibia. There was a Kernig, rigidity of the neck, no Macewen, excretions involuntary.

February 15. Patient could hear; was more rational; had external strabismus of right eye; this was noted the previous day; rigidity of neck still present; as also Kernig; had normal reflexes on both sides; some edema of the tibia.

February 16. Patient improved; more rational; Kernig and rigidity still present; the urine was normal.

February 17. Patient sat up; was quite rational; external strabismus of the right eye unchanged; Kernig still present; headache of the day before was gone.

February 19. The patient continued to improve; no apparent paralyses of the extremities; no paralysis of facial muscles.

February 22. The patient complained of lack of power of left hand; right grasp a little stronger; no limitation of motion of upper extremities; no apparent atrophy.

February 24. Slight limp in left leg, knee-jerks on left side diminished.

February 25. Patient looked bright; felt well; slight Kernig; slight weakness of left upper extremity.

March 2. Patient examined to-day; appeared bright and normal; slight loss of power in left hand; no atrophy of muscles visible in upper and lower extremities; no loss of power; no Kernig; no Babinski; no ocular or facial

paralyses. Patient had loss of power in left arm, but this was more apparent than real.

The temperature of the patient, which from admission February 8 to February 14 ranged up to 104 F., gradually fell on February 14 to 100 F.; respiration became pretty regular—from 22 to 32—and the pulse was 90 to 120. The following day the temperature, pulse and respiration were normal.

The night nurse reported that on admission and at intervals afterward the child was particularly noisy at night. During the day she was quite comfortable. The urination was almost always involuntary. She refused nourishment, was constipated up to February 12, after which time she slept at night and was quiet. The puncture fluid was reported as practically normal; there was sugar present, also traces of albumin; cytologic examination showed a few mononuclear cells. Wassermann was negative. The urine was obtained by catheter and, with the exception of a few bacterial cells, was sterile.

Examination of Urine.—February 11, hyaline and granular casts, and some blood and pus were present. February 12, about the same—blood, pus and casts. February 14, a few granular casts. February 15, no casts and no blood; negative after that time with the exception of a few leukocytes.

Discussion.—In this case the onset was acute, there then was a remission in symptoms and then the patient took to bed after a week with all the symptoms of a meningitic attack; in fact, when seen in consultation a cerebrospinal meningitis was suspected, and a puncture was made with that diagnosis in view, but the fluid obtained was clear and nothing found but a lymphocytic cytology. There was a high leukocyte count of the blood, including an excess of polynuclear cells. The illness ran the course of an acute meningitis. The finding in the urine corresponds to that of Wickman in one of his cases. Inasmuch as the urine cleared up completely, it must be surmised that the nephritis was only part of a general infection. The patient fully recovered, with a strabismus due to ocular palsy remaining with slight weakness in the left upper extremity. This, I think, is a case of acute polio-encephalitis with a meningitic onset, its course closely simulating cerebrospinal meningitis of the epidemic type. The patient was not discharged until she had absolutely recovered.

CASE 5.—Female, aged 5, was admitted Oct. 14, 1909.

Family History.—Father suffered from pulmonary tuberculosis; mother and nine other children healthy.

Previous History.—The patient was born at full term; no instruments used; measles at 2½ years; no complications; whooping-cough just previous to measles. The patient had a moderate dry cough since having measles up to one year prior to admission. No convulsions, no ear symptoms, bowels regular, urination normal. About sixteen months before admission the patient was operated on for acute appendicitis; ill five weeks; healthy since until present illness.

Present Illness.—Present illness began four days prior to admission, when the mother noticed that the child became drowsy, lost interest in her surroundings and developed moderate fever. The next day the child vomited for the first time. The vomitus consisted at first of undigested food; later of small amounts of bile-stained fluid, accompanied by much retching; vomited since, chiefly after taking food.

Since the onset the bowels were obstinately costive; no marked abdominal distension, no blood or mucus in stool. Drowsiness became intensified; child

would start in her sleep with a shriek; sighed considerably. The day before admission the child complained of pain in back of neck, developed some rigidity and became delirious and irrational; no convulsions, no palsies, slight dry cough, no dyspnea; marked prostation; drowsy; responded when disturbed; was irrational and delirious; respiration irregular; no head retraction; neck was rigid; general hyperesthesia; Macewen present, especially on left side; marked photophobia. Eyes, ears and mastoids normal; skin showed scar of operation; *tâche cérébrale* present; scattered papular spots; a few small lymph-nodes in left axilla; tongue, dry and coated; throat, teeth and gums in good condition; chest well formed; lungs clear; heart borders normal; action regular, rapid, of poor force, sounds clear, no murmurs; pulses equal, regular, rapid, small.

Liver and spleen not enlarged; abdomen lax; reflexes present.

Extremities.—Kernig's sign present on left side; left, Babinski at times.

Synopsis.—Fever, drowsiness, delirium, hyperesthesia, rigidity of neck, Macewen, left Kernig.

Blood Count.—White blood cells, 21,000; polynuclears 61 per cent.; small lymphocytes 28 per cent.; large lymphocytes 11 per cent.

October 15. Lumbar puncture; 24 c.c. clear, colorless fluid under increased tension withdrawn.

October 16. This morning patient was semiconscious; roused when talked to; athetosis in hand; dry, coated tongue; talks with lisp; slight flatness of left side of face; Kernig on both sides; marked rigidity and tenderness of neck; slight Macewen on left side.

October 17. Lungs negative; paresis of left side of face more marked; marked rigidity of neck; marked Kernig on both sides; fundus examination of eyes was negative; patient semiconscious. Von Pirquet positive.

October 18. More conscious; Kernig; Macewen very slight on left side; slight internal rotation of left eye; marked neck rigidity.

October 23. Von Pirquet still evident; Kernig, left facial flatness; bromic eruption on legs; could sit up; rigidity of neck almost gone; tongue moist; Macewen not elicited.

October 25. Sat up; left side of face still slightly flat; neck supple; Kernig, 30 degrees on both sides.

October 24. Urine amber, acid, specific gravity 12, albumin 0; a few white blood cells.

November 4. Urine amber, acid, specific gravity 24, albumin 0; a few white blood cells.

October 15. Cerebrospinal fluid showed lymphocytes 100 per cent.; negative for bacteria; no growths; no tuberculosis; albumin .5 mm.; sugar reducing substance present; Widal negative 1 to 20, 1 to 50; also on October 18.

October 14. Temperature 104.2 F. on admission; dropped to 100.8 F. on following day; and on sixteenth reached 99 F.; slight rises to 100 F. afterward. Pulse 116 on admission, respiration 28. Weight 45¾ pounds.

Discussion.—This patient, 5 years of age, was attacked more or less acutely with high fever and vomiting, passed into a condition of sopor which became intensified after a few days. There was the picture of meningitis with fever, drowsiness, delirium, apathy, vomiting, constipation, pain in neck and rigidity of the neck. What was especially disquieting was a positive von Pirquet cutaneous reaction to tuberculin, which misled into the diagnosis of tuberculous meningitis. The subsequent complete recovery disproved this, leaving us to infer a latent glandular tuberculosis. The fluid obtained by lumbar puncture showed nothing more than a marked lymphocytosis.

The recovery of this patient was complete, there being left only a slight facial flatness; no real paralysis. The temperature after the first day following admission to the hospital was normal; the urine was normal; the fundus oculi was normal.

CASE 6.—This case resembles a case I saw recently in consultation, a girl of 13. The girl was seen by several physicians, all being quite positive in the diagnosis of tuberculous meningitis. This girl like the case I am to depict recovered, with the exception that she did not, as in this case, yield a positive tuberculin reaction.

History.—The patient was a boy, aged 4, admitted to my hospital service. He had had measles, scarlet fever and diphtheria.

Present Illness.—This began three weeks before with an attack of fever and vomiting and headache; following this the boy became drowsy, did not notice and was soporose and stupid. The condition of drowsiness became more and more marked, and in this condition he was brought to the hospital. The patient was well nourished, had some slight hydrocephalus, staggered when upright, swayed especially to the left when he walked and threatened to fall. The patient was in a trance-like state and sat up in bed staring ahead; he slept well. The examination of the fundus oculi was negative.

The patient's urine at first contained acetone, diacetic acid and a trace of sugar. These disappeared in the first two days of the hospital stay. After three weeks of illness the above symptoms cleared and the patient was well. There was from the first a positive tuberculin skin reaction (von Pirquet). No lumbar puncture was made. This case differs from that of the girl I just mentioned, inasmuch as the latter had no tuberculin reaction and was unable to sit up or stand without experiencing marked vertigo. The girl was highly hyperesthetic, whereas this symptom was absent in the boy.

CASE 7.—C. R., aged 5½, was admitted Jan. 10, 1911.

Family History.—Negative.

Previous History.—Had pneumonia and measles one year ago; no other diseases. The child was perfectly well until thirteen days before admission.

Present Illness.—This began thirteen days previously with vomiting and headache. The child vomited one to three times practically every day since onset; vomiting was not projectile in character, having no relation to meals. Headache had been frontal in location and almost constant in character; had slight fever following the onset; for a week had occasional cough, with slight mucopurulent expectorations. For two days the father noticed that the child had been drowsy most of the time, and was rather irritable when awakened. There were no disturbances of the special senses; no paralyses noted; no ear disturbances; bowels fairly regular; urination normal; appetite poor; no symptoms of cardiac or renal disturbances.

Synopsis.—Vomiting and headache for three days, slight fever, slight cough; drowsiness for two days.

Physical Examination.—General condition good; well nourished; irritable. Head—no rigidity, no Macewen. Eyes—pupils equal; react to light and dilate, no palsies. Ears and mastoid negative. Mouth and teeth—several upper teeth missing; otherwise in fair condition; tongue moist and coated; throat congested. Glands and skin negative; chest well formed, expansion good; lungs negative; heart, regular, good force, no murmurs; liver—fifth space, sixth rib to free border; not felt; spleen not felt. Abdomen held tense; tympanitic; no masses; abdominal reflexes not obtained; slight *tâche.*

Extremities.—Knee-jerks much exaggerated; no Kernig, no clonus; Babinski and Oppenheim, bilateral; patella-jerk bilateral; tremor of upper extremities.

Genitals.—Some reddening of vulva; no discharge. Rectal examination not made.

Synopsis.—Irritability, exaggerated knee-jerks, Babinski, Oppenheim, tremor of upper extremities.

January 11. White blood cells 31,200; polynuclears 80 per cent.; lymphocytes 18 per cent.; large mononuclears 1 per cent; basophils 1 per cent.

January 12. Ears negative. Lumbar puncture made; about 30 c.c. of clear fluid and flakes withdrawn.

January 13. White blood cells 21,200; polynuclears 80 per cent.; lymphocytes 14 per cent.; large mononuclears 5 per cent; easinophils 1 per cent.

January 16. General condition better; child brighter; slight rigidity of neck persists; no Kernig.

January 22. Inner reflexes present; child will not stand; eyes closed; uncertain gait present.

January 24. Child had been picking up but complained of pain in extremities; reflexes increased; Kernig present; resents interference; no pain in back; no headache.

White blood cells 10,600; polynuclears 73 per cent; small mononuclears 26 per cent.; large mononuclears 1 per cent.

February 7. Patient up and about ward.

The temperature during the first week of the hospital stay ranged from 99 to 101 F. and then dropped to the normal.

Urine during stay in hospital at only one time showed a few hyalin casts.

The fluid obtained by lumbar puncture contained 90 per cent. lymphocytes and 10 per cent. polynuclear cells. Smears and culture negative as to bacteria; sugar, moderate reduction; some albumin.

Discussion.—The onset was sudden, with headache and vomiting daily, slight fever with cough, and after ten days, increasing sopor and irritability. On admission to the hospital there were no palsies, but there was the mental irritability, exaggerated reflexes with tremors of the extremities. The blood showed during the illness a marked polynuclear leukocytosis with a lymphocytic picture in the spinal puncture fluid.

I have thus described a condition which is of great interest. It is apt to be, and is constantly, mistaken for meningitis of the cerebrospinal, acute suppurative or subacute tuberculous form. The onset of the illness is acute; it begins with a previous history of absolute health. After the acute symptoms set in there may be in some cases an abatement and then a recurrence of symptoms of a cerebral nature, which gradually deepen. If the case is one resembling an acute meningitis, the symptoms are more active, with neck rigidity, pain in the neck, headache and delirium. If the case resembles the tuberculous form of meningitis, the patient lies more quietly, exhibits palsies of the cranial nerves, and may even have marked hydrocephalus with distinct Cheyne-Stokes respiration and unconsciousness. In both sets of cases the delirium, sopor or coma lightens, the patients after a week or more of illness become brighter, and recovery proceeds. Lumbar puncture in all the cases reveals a clear or slightly flocculent fluid, without bacteria, and a cytology of 90 per

cent. to 100 per cent. lymphocytes. An examination of the blood shows at first a leukocytosis of pronounced degree of the polynuclear type.

The onset of the disease may be ushered in by fever, which rapidly subsides to within a fraction of a degree of the normal and the major part of the illness runs its course with this temperature, which is practically normal. The diagnosis is made from the points of clinical course laid down in this paper. The prognosis is for the most part good, except in those cases which involve the nuclei of the nerves controlling respiration. In such cases the outlook is that of an acute bulbar paralysis, when the extent of the lesion will decide the fate of the case. The main point is to have in mind the great similarity of a certain set of these cases to those of tuberculous meningitis, and acute cerebrospinal meningitis, and the absolute futility of a positive diagnosis without study of the case, lumbar puncture and all the clinical aids at our command.

The fatal cases of the cerebral forms of polioencephalitis have been mentioned in this paper. I have two cases of this kind to report, in one of which autopsy was performed and the diagnosis of polioencephalitis confirmed. These cases may be of sudden onset with cerebral symptoms, and a rapid involvement of the bulbar nuclei. The result is a picture of acute bulbar paralysis with cerebral onset. In some cases the onset may be gradual, in others acute. The paralysis involves the muscles of deglutition and phonation and this is the first sign of bulbar involvement of a serious nature. In these cases the ocular and facial nuclei may be involved, and as the process spreads down there is a complete paralysis of a descending type, involving the muscles of respiration. In one of the cases the respirations seemed to cease first while the heart continued beating. All cases here recorded were fatal cases, but this must in no way be assumed to be always the case, because I have seen a few bulbar cases recover, one notably in a child 3 years of age, in which the respiration was involved, as was also deglutition. In this case a complete recovery occurred.

CASE 8.—A. B., male, aged 5, was admitted Oct. 4, 1908.

Family History.—Father had tuberculosis in 1905 when at Bedford Station; since then was well. He had lost 5 pounds in the previous few weeks. The mother and two other children were well.

Previous History.—The patient had measles two years ago; otherwise no illnesses; bowels always regular; appetite good; mentally bright; never complained of headache; eyes and ears good; no eruptions on skin.

Present Illness.—Onset one and one-half weeks prior to admission, with indefinite symptoms. It was noted that the child was weak and lackadaisical; did not complain of headache; had no convulsion or palsies; had some fever; appetite was good; child slept uneasily at night and cried out in sleep; bowels regular; in the previous four days the child began to cough when talking; had difficulty in swallowing; regurgitation and coughing back food mixed with mucus; had been unable to talk in this time; unable to sit up or walk; ears and eyes remain functionally unaffected; complained of slight pain over heart; cried out frequently in sleep and had involuntary movements of arm.

Physical Examination.—General condition fair; patient well nourished; lay in an apathetic condition; cheeks flushed; moderate dyspnea; child was hoarse; marked gurgling in throat; alæ nasi dilate with each inspiration; child responds when spoken to; voice thick and husky; moderate rigidity of neck; on bending neck child was irritated; Macewen on left side; no irregularity of skull; no definite tenderness made out; no retraction of head; child somewhat irritable; Kernig; *tâche cérébrale* present; moves arms and lower extremities, but acts as if in trance; answers monosyllabic.

Skin and mucous membranes had a good color; ears and mastoids externally negative; moderate amount of cerumen in canal; eyes and upper lids somewhat closed so that upper one-half of pupil was covered. This could be overcome and child raised lid in normal manner. Pupils: right slightly larger than left, regular, central moderately dilated; reacted somewhat sluggishly to light and accommodation; weakness of both external recti; conjunctivæ negative. Nose—evidences of slight secretion ali nasi; otherwise negative. Face—left-sided facial paresis. Mouth, teeth and gums in poor condition; tongue thickly coated and moist; tonsils hypertrophied. Throat—uvula elongated; throat slightly ingested; palate moves slightly. Larynx, trachea, thyroid, spine, bones and joints negative; a few small cervical and inguinal glands were palpable.

Chest was well formed and symmetrical; right chest seemed to expand slightly more than left; no retraction.

Lungs: Anteriorly there was some dulness over the right axilla; marked bronchial râles over entire chest; breathing over anterior chest was exaggerated; numerous loud gurgling râles and expirations which seem to be transmitted from trachea. In the right axilla there were a few mucus râles on inspiration; posteriorly there was dulness at right apex down to about two fingers below spine; dulness at left apex of similar extent; over entire chest posteriorly there were numerous bubbling râles on inspiration and expiration; most marked at left base; breathing harsh and exaggerated; no change in voice.

Heart: Right border at right border of sternum; left border in nipple line; visible beat at fourth rib; apex neither seen nor felt; sounds clear; no murmurs; action regular; good force; somewhat accelerated.

Abdomen: Somewhat retracted and lax; no pain or tenderness. Liver, fifth rib to sixth rib; free border not felt; spleen not felt.

Extremities: Upper, grips seem to be equal; child seems to use left hand more than right, although both can be used fairly well; right arm weaker than left; no impairment on passive motion; no atrophies; arm reflexes present. Lower slight edema; knee-jerk not obtained; no clonus; no Babinski; no paresis or paralysis of legs.

Genitals: Double cryptorchidism. Rectal examination not made.

Blood: Leukocytes 25,000.

October 15. Eyes examined and found negative.

The child's condition remained about the same; lay quietly, preferably on the right side; child gets frequent attacks of dyspnea, which were accompanied by loud breathing; on auscultation there were found numerous moist gurgling râles throughout the chest; child takes nourishment very poorly, owing to the difficulty which it has in swallowing; reflexes in extremities gone.

October 16. Condition remained the same; lay quietly; eyes half open; had some photophobia and could see objects readily; had slight weakness of the external and internal recti muscles of the eyes; could not swallow; regurgitated all food given by gavage; breathing remained the same; signs of pulmonary edema came on frequently and cleared up in a large measure after hyperdermic injection of atropin. It was necessary to resort to rectal feeding. Lower extremities had no reflexes; abdominal reflexes also gone; there was no Kernig; electrical reactions and sensations not yet tested.

Blood: Leukocytes 33,000.

Urine: Hyalin casts; few granular casts.

The patient died with signs of respiratory failure. Postmortem made.

CASE 9.—G. R., female, admitted November 4, 1910.

Family History.—Seven other children, all well; father coughs; no tuberculosis.

Previous History.—The patient had measles; no other disease; no cardiac, pulmonary or renal disease, no rheumatism. Previous to present illness the child was perfectly well and played about in the street.

Present History.—At 5 o'clock a. m. on the morning of admission the child had involuntary urination while in bed; on taking her up she squirmed about and screamed; it was then noticed that the child could not articulate and could not stand on its feet; vomited once in the morning, and whenever she was given anything to eat; appeared to have some difficulty in swallowing; all day the child lay quietly in bed without moving a limb; had no fever.

Physical Examination.—General condition good; patient well nourished; flushed facies; markedly apathetic; somewhat stuporose; respiration somewhat rapid and regular; does not cry nor give response to spoken language; neck, no rigidity, no mastoid; Macewen present; distinct flatness of right side of face; right palpebral fissure not completely closed; mouth drawn to the left.

Eyes: Pupils equal, central and regular; mucoid discharge from conjunctivæ; no corneal anesthesia; no petechia or palsies; dry crusting of nose; lips of good color; tongue somewhat coated; gums in good conditions; teeth in good condition; pharynx negative; palate, slight deviation to left; moves actively; skin, clear, good color; one or two small healing scars.

Glands: Submaxillary, post cervical, chains.

Chest: Well shaped; lungs, negative; heart, borders not enlarged; apex, fourth space within nipple line; action rapid and regular; pulse, equal, regular, rapid.

Abdomen: Negative; liver, fourth to sixth ribs; spleen not felt.

General: Patient unable to hold back up; head falls weakly to side; weakness of right side of body complete; right arm useless; left knee-jerk just present; left arm tendon reflex exaggerated; right knee reflex elicited with difficulty; right arm completely relaxed; apparently no power; slight redness of vulva.

November 6. Patient in a condition of apathy; the Macewen still quite marked, more so than the previous day; right facial paralysis marked; a little weakness of external rectus of right side; complete right hemiplegia; knee-jerks absent on paralyzed side; present on left side; considerable atrophy of the right deltoid, biceps and triceps; sighing respiration; *reaction of von Pirquet 2 mm. positive;* slow, forcible heart action; child vomited once; constipation present; swallowed with difficulty; refused nourishment; did not talk; a little lagophthalmus of right eye.

November 4. Von Pirquet; white blood cells 17,600; polynuclears 82 per cent.; small lymphocytes 16 per cent.; small mononuclears 2 per cent.

There was a slight difference in size of the thighs, the affected being smaller; exaggerated reflex of left affected extremity; only occasionally obtainable on right side; weakness of the muscles of the neck; head fell back; child could sit up.

November 6. Right knee-jerk this morning easily obtainable; left knee-jerk elicited with difficulty; left triceps-jerk exaggerated; right not obtained.

November 7. Heart continued beating after respiration ceased. Temperature ranged from 100 to 104.8 F.; at death 102.5 F.; pulse 96 to 130; respiration 24 to 36.

Fluid obtained by lumbar puncture: First puncture had lymphocytes too few to count; no bacteria; animal inoculated. Second puncture: Cytology, 72 per cent. lymphocytes, polynuclears 28 per cent.; negative to bacteria; albumin 1 mm.; sugar, slight reduction.

Blood culture, negative.

30 East Sixty-Second Street.

INFANTILE PARALYSIS: SPINAL FORM*

JOHN LOVETT MORSE, A.M., M.D.

It hardly seems necessary to consider in detail the symptomatology of the ordinary classical type of the spinal form of infantile paralysis. Everyone knows how varied the onset may be and how much difference there is in the severity of the constitutional symptoms. It is common knowledge that the paralysis comes on quickly in the course of a few hours, or at most in three or four days; that there is then a stationary period of from one to four weeks, which is followed by a period of improvement lasting from six months to perhaps a year, and that the final paralysis is always less than the initial. The improvement in the paralysis is due to the facts that many of the ganglion cells, which at the height of the disease are merely compressed or only partially involved, recover their function, wholly or in part, and that the nerve-supply of a muscle never arises from a single segment of the cord.

It is impossible, therefore, in the acute stage to prophesy how extensive the final paralysis will be. Recovery is sometimes nearly or quite complete when the initial paralysis is very marked, while at other times there is very little improvement, even when the original paralysis is slight. On general principles, however, the greater the extent of the initial paralysis, the later the beginning of the stage of retrogression and the slower its progress, the greater is the final paralysis.

The final paralysis is, as a rule, monoplegic or hemiplegic, seldom diplegic or paraplegic. It seems idle, however, to give statistics as to the relative frequency with which the different extremities are involved or to detail the possible combinations, because these facts are of no practical importance in the individual instance. It is comparatively unusual, however, to have all the muscles of an extremity involved or, at any rate, involved to the same extent. In most instances some of the muscles are spared and in many only one or two are affected. The grouping of the paralyzed muscles has, moreover, no relation to their physiologic function, the distribution of the paralysis in many instances appearing most peculiar. The peculiar distribution of the paralysis is easily understood, however, when it is remembered that the nerve-supply of a given portion of an extremity, the forearm, for example, does not all arise at the same level of the cord, that the blood-supply of the cord is horizontal, not vertical, and that the affection of the cord is due to interference with the

* Read at the meeting of the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

blood-supply, resulting from inflammatory processes in the vessel walls, due to infection originating in the subarachnoid space.

It is not very unusual for other muscles than those of the extremities to be involved, while these escape. Such muscles are most often the erectors of the spine and the abdominal muscles. The involvement is, moreover, not infrequently unilateral. The paralysis is, for example, sometimes limited to the extensor muscles of the neck, to the muscles of one side of the spine, or to those of one side of the abdomen. Paralysis or paresis of these muscles is often overlooked and the deformities to which they give rise attributed to other causes. Scoliosis from this cause is very often misinterpreted and enlargement of the abdomen from paralysis of the abdominal muscles is attributed to indigestion with flatulence, or to ascites. In one patient whom I saw, a unilateral paralysis of the abdominal muscles had been mistaken for an abdominal tumor. Incidentally, the prognosis in paralysis of the abdominal muscles is fairly good.

THE PROGRESSIVE TYPE

In a certain number of instances the paralysis is of the progressive type. It usually begins in the lower extremities and gradually extends upward, resembling in its course that of the so-called "Landry's paralysis." It is probable, in fact, that a very considerable proportion, if not all, of the cases which have in the past been described under this name were really cases of infantile paralysis. When the paralysis reaches the external muscles of respiration, as it not infrequently does in this type, a fatal outcome is practically inevitable. In certain cases the phrenic nerve is also involved. Death occurs sooner, of course, when this happens. This form must not be confused with that in which death results from respiratory paralysis due to the involvement of the centers of respiration in the medulla. In other instances the paralysis begins in the arms and extends both downward to the lower extremities and upward to the centers in the medulla.

THE POLYNEURITIC TYPE

Pain is a prominent symptom in many instances. It is, in fact, so common that it is hard to understand how the old dictum that there is no pain in infantile paralysis ever originated. The pain is sometimes in the joints, but more often along nerve-trunks, or is indefinite in its distribution. It is usually most marked in the paralyzed parts. There is occasionally tenderness over the nerve-trunks. Pain and tenderness are at times marked enough to cause the paralysis to be entirely overlooked and a diagnosis of rheumatism or scurvy to be made. The extremities are often held rigidly and all motions as vigorously resisted as possible because of the pain on motion. This combination of rigidity and resistance is possible, of course, only when the muscles are but partially para-

lyzed or when some of them are intact. The failure to appreciate the significance of this condition of combined flaccidity and spasticity has led, in my experience, to many errors in diagnosis during the acute stage. In one of my own cases it was necessary, on account of the rigidity of the leg and the pain which attempted motion caused, to give ether enough to dull sensation before it could be determined whether the trouble was an infantile paralysis or a disease of the hip joint. When pain was no longer felt the affected extremity was flaccid while the muscular tone was normal in the rest of the body.

ABORTIVE TYPE

There is no doubt that the disease occurs very frequently without the development of any paralysis. The term "abortive" ought strictly, of course, to be limited to the cases in which there is no paralysis. There is, however, another class of cases, in which the paralysis is very slight and lasts but a few hours or days, which is on the border-line between the abortive type and the ordinary spinal type. These cases are very easily overlooked clinically unless the symptoms are very carefully studied.

DIAGNOSIS

The diagnosis of infantile paralysis of the spinal type after the development of the paralysis is, of course, very easy. The great difficulty at present lies in making the diagnosis before the appearance of the paralysis. Sweating, marked nervous irritability and hyperesthesia are present in many instances before the onset of the paralysis, but they are not at all constant. If they are present, they are strong evidence in favor of infantile paralysis, but their absence does not count against it. Hyperesthesia is the most constant and the most important symptom of the three.

Although leukopenia occurs in animals during the early part of the acute stage of infantile paralysis, it is certainly not a constant symptom in man and in many instances is replaced by a hyperleukocytosis. Further experience is necessary to determine of how much value the leukocyte count is in the early diagnosis of infantile paralysis. At present it is of little or no assistance. While it is possible that there is a lymphocytosis in the early stages of infantile paralysis, there is at present not sufficient evidence to show whether either a relative or an absolute lymphocytosis is at all a constant phenomenon. If further investigation shows that it is, it should be of considerable assistance in the early diagnosis.

Experimentally, there is an increase in the number of cells in the cerebrospinal fluid during the prodromal stage before the appearance of the paralysis. The polynuclear cells at this time exceed the mononuclear. After the appearance of the paralysis the mononuclear cells quickly out-

number the polynuclear. A fibrin clot is often formed in the prodromal or early part of the acute stage. Frissell, in the only instance in which lumbar puncture has been done in man during the preparalytic stage, obtained a slightly opalescent fluid which gave a marked protein reaction with Noguchi's test and showed an excess of polynuclear cells. The formula had begun to change to the lymphocytic, however, before the paralysis developed. Lumbar puncture ought, therefore, to provide a most valuable means of diagnosis in this disease during the preparalytic stage. Its value is considerably limited, however, by the fact that there is nothing whatever characteristic about the early symptoms of infantile paralysis, and, therefore, nothing to definitely suggest its use. In order to recognize the disease early, therefore, before the onset of the paralysis, it would be necessary to do a lumbar puncture on every sick child, which hardly seems a rational procedure.

During the acute stage of infantile paralysis the cerebrospinal fluid is clear, not infrequently under somewhat increased pressure, often forms a fibrin clot on standing, and always contains an excess of cells. These are chiefly of the mononuclear type, most of them being lymphocytes. These changes are, however, identical with those found in tuberculous meningitis, the disease with which it is most likely to be confounded. An increased protein content is also found by the Noguchi test in both diseases. A positive diagnosis between them can only be made, therefore, by the examination of the cerebrospinal fluid for tubercle bacilli. These can be found in the great majority of the cases of tuberculous meningitis if the examination is careful enough. They are more than likely to be missed, however, in the ordinary routine examination. The characteristics of the cerebrospinal fluid in infantile paralysis are, of course, so different from those in meningococcal, influenzal and pneumococcal meningitis that no confusion with these conditions is possible.

The only possible method of making the diagnosis of infantile paralysis of the spinal form before the onset of the paralysis is, therefore, by lumbar puncture. In order to be of much assistance, however, this must be done very generally in sick children during the summer months, because there is nothing characteristic and usually nothing even suggestive about the early symptoms.

70 Bay State Road.

THE CONTROL OF EPIDEMIC POLIOMYELITIS *

SIMON FLEXNER, M.D.
NEW YORK

Epidemic poliomyelitis has, since its appearance in 1907-08 along the Atlantic seaboard, extended over the entire United States. This wide distribution has fortunately not been attended by a regular and uniform prevalence of the disease in all communities. Indeed, considerable territories would seem to have escaped its ravages, although few, if any, of the states have remained entirely free from invasion. The number of persons attacked can be only conjectured, but it is probable that it reaches into the thousands. The mortality has been the average noted in the European epidemics, and has approached 10 per cent. Undoubtedly the mild or abortive forms of the disease have prevailed along with the severer paralytic types, and in many instances their nature has been certainly overlooked. Among the paralytic cases all grades of the affection have been encountered, and the number of cases in which complete recovery without residual paralysis has taken place would appear to have been not inconsiderable. In other words, the American epidemic of poliomyelitis is in agreement with the earlier European epidemics in all essential respects, and differs from them only by reason of its wide distribution and great total number of cases. This variation is to be explained probably not by supposing that the conditions for the prevalence of the disease in the United States were more favorable than in Europe, but because of the greater extent of territory embraced under one government. Possibly also the United States have suffered disproportionately and more severely than European countries because of the failure, in many communities, to make prompt recognition of the nature of the malady, and because of the want of a body of authoritative sanitary regulations that could be put into rapid operation in the effort to delimit the spread of the disease through the employment of methods of quarantine. I am convinced that the disease in some communities was mistaken for periods of many months for epidemic meningitis, a fact not highly surprising in view of the lack of general knowledge regarding epidemic poliomyelitis that existed throughout the country, and in view of the common occurrence of marked symptoms referable to meningeal irritation in the course of the malady.

---

*From the Laboratories of the Rockefeller Institute for Medical Research.

*Based on remarks made before the Association of American Physicians at Atlantic City, May 9, and the American Pediatric Society at Lake Mohonk, New York, June 1, 1911.

The question of the control of epidemic poliomyelitis is one of high interest at the present time. This control may be of two kinds, namely, that effected through the employment of measures of prevention, and that through the employment of modes of treatment. Of the two possible means of control, the first, that through prevention, is to be given the place of prime importance, for it is not only more humane and scientific to prevent a disease rather than to effect its cure, but in the present instance the knowledge available makes prevention a possible achievement, while there exists no known means of therapeutic control worthy the name.

The measures of prevention employed should be those based on knowledge of the mode of infection that clinical observation and experimental investigation have thus far supplied. At any given period we can apply intelligently and with confidence only those preventive measures that are founded on such knowledge. It would seem to be established that the human agency of transfer of the infectious agent does occur and perhaps frequently. Moreover, this human agency includes not only the actively infected or ill, but also healthy persons who perform the part of intermediaries between the stricken and the well who are to develop the disease. To express this point in somewhat more technical language, we must accept for the present the existence of both active and passive carriers of the infectious agent of epidemic poliomyelitis and accord to each a share in the distribution of the agent through the implantation on other susceptible persons. Hence, in the effort to control this distribution, there should be employed adequate measures of isolation and quarantine of the sick as well as those in immediate attendance on the sick.

We are not sufficiently accurately informed of the period of survival of the infectious agent within the active and passive carriers to enable us to state precisely what the period of quarantine should be. We possess some data, not, however, overaccurate and convincing, based on the period of development of secondary cases of the disease, that suggest that the virus may persist in the infected in an active state for several weeks, and we further possess experimental evidence to the effect that in inoculated monkeys the virus may survive in the mucosa of the nasopharynx at least for several weeks and even several months (Osgood and Lucas, Flexner and Clark). This long period of survival in the monkey would, however, appear to be exceptional. In many instances the virus cannot be discovered in the mucosa as early as one, two or three weeks after the appearance of the paralysis (Flexner and Clark). I am disposed, therefore, to view the examples of long persistence of the active virus in the monkey, with which, doubtless, corresponding examples among human beings will be found, as the equivalent of the chronic carriers of bacteria among men and animals in other well-established types of infectious diseases. Such chronic carriers constitute not only and fortunately an exceptional class, but in framing our practical measures of prevention we have considered them, up to the present time, in rather

an incidental way. Thus, for the present it would seem that a period of isolation of from three to four weeks would be sufficient in ordinary cases of epidemic poliomyelitis, it being understood that when the acute or febrile course of a case of the disease is prolonged, the period of isolation be lengthened accordingly.

The efficiency of any group of preventive measures will depend on the directness with which they deal with the source of the infectious agent that they seek to restrain. We have progressed very far into the management of an infectious disease when we have learned the portals of egress and of ingress of the infectious agent. Such knowledge of this kind as we possess regarding epidemic poliomyelitis is based wholly on animal experiments, and hence the degree of its application to human beings has still to be established.[1] It has been shown that in the monkey the virus of poliomyelitis passes from the central nervous system into the nasal mucosa, and it has been found that monkeys can be infected more readily by applying the virus to the nasal mucosa than by any other means except direct intracerebral inoculation. It is for this reason that I believe special attention should be accorded the nasal and buccal secretions of persons affected with epidemic poliomyelitis during the period of isolation, and even for a period afterward. The facts known concerning the relation of the nasal mucosa to the virus of poliomyelitis must be taken at precisely their true value, and must not be considered to exclude other modes of infection by way of other channels in human beings. Hence beside the attention given to the destruction of the nasal and buccal secretions, and to the keeping clean and free from these secretions the hands and other parts of the body as well as the clothing, vigilance should not thereby be relaxed in dealing with all the secretions in a sanitary manner.

Studies of the manner of travel of and the route taken by the disease in thinly populated districts especially have failed in not a few instances in supporting fully the idea of the human agency in the transmission of the infection. Studies of this kind cannot be made satisfactorily in cities or even in towns for the reason that the contact with persons is too frequent and promiscuous to permit of accurate tracing. Owing to this discrepancy, some other agencies have been invoked to account for the transmission of the infection over wide areas, and the chief ones of this character have been domestic animals and insects. Paralytic diseases among domestic animals are known and not highly infrequent. They have been noted among dogs, horses and fowl, but thus far it has not been found possible to correlate the paralytic diseases of the lower animals and those of man. Perhaps the most frequently observed coincidental paralytic diseases have been between hens and human beings. Undoubtedly since the wide prevalence of epidemic poliomyelitis, the existence of a

1. Since this was written Landsteiner, Levaditi and Pastia (Semaine Medicale, 1911, No. 25, p. 296) have established the presence of the virus of poliomyelitis in the tonsils and pharyngeal mucosa of a child who succumbed to infantile paralysis during the acute stage of the disease.

paralytic disease among barnyard fowl has been more commonly noted. Possibly the condition has not actually become more frequent, but owing to the circumstance mentioned it has been oftener observed. It would appear that the paralysis among fowl is caused not by lesions of the central nervous system, but by lesions of the peripheral nerves and that it is due to a peripheral neuritis. It has not been found possible to transmit by direct inoculation the paralytic disease from chicken to chicken, or from chicken to monkey, or from paralytic monkey to chicken (Flexner and Lewis). However, it has been found possible to develop the paralysis in the laboratory by keeping the chickens in confinement for some time, and by supplying them an unusual and doubtless improper form of food (Flexner and Clark). It has proved as little possible to transfer the paralytic affection of dogs from one individual to another by direct inoculation or from dog to monkey or from paralyzed monkey to dog (Flexner and Lewis). These failures do not, of course, exclude the possibility that a reservoir for the virus may exist among domesticated animals that do not even respond to its presence by developing paralysis or other conditions which could be recognized as resembling poliomyelitis in man. The manner of the action of the virus of poliomyelitis in rabbits provides an illustration which shows how necessary it is to avoid general deductions in this field. At first it was strenuously denied that rabbits could be infected at all with the virus of poliomyelitis, and the examples of supposed successful inoculation reported were entirely disbelieved (Krause and Meinicke, Lentz and Huntemüller); but it must now be accepted that young rabbits occasionally, but by no means generally, are subject to inoculation with the virus of poliomyelitis, at least after it has passed through a long series of monkeys (Marks). Apparently a small percentage only of the inoculated rabbits develop any obvious symptoms, and these die, as a rule, during convulsive seizures which come on suddenly. A given virus has up to the present been sent through a series of six rabbits, after which it has failed to be further propagated. From the sixth series it has been reimplanted on the monkey, in which animal typical paralysis has been produced (Marks). It remains to add that the rabbits which succumb to the inoculation do not show any characteristic lesion of the central nervous system or other organs, as far as has been determined. The monkey, on the other hand, invariably shows the typical lesions of the central nervous system.

Insect contamination with the virus would serve, were it proved not only to be an experimental possibility but to occur in nature, to clear away any present apparent discrepancies in the epidemiology of the disease. In this connection it should be stated that not only does epidemic poliomyelitis spread over a wide territory, but its spread is not promiscuous, but along the routes of human travel. Therefore insects that seek human habitations and routes of travel, that possess the power to migrate over a considerable territory, that affect all classes of society,

that abound during the period of greatest prevalence of the disease, and that do not wholly disappear at any season, should be the first to come under suspicion. Many, if not all, of these conditions are fulfilled by the common house fly.

Laboratory-bred flies have been subjected to contamination experiments with the virus of poliomyelitis, from which it appears that they are capable of harboring the virus on their bodies in a living and infectious state for at least forty-eight hours. Moreover, it has developed that the virus also survives within the viscera of the insects for some time. (Flexner and Clark.) It should now be readily possible to secure flies from rooms in which cases of acute poliomyelitis are, in order to ascertain whether in nature they also become contaminated with the virus of the disease.

When we turn to the question of the control of poliomyelitis by the cure of the disease we refer of course to the reduction in the mortality and in the crippling effects which it causes. In respect to this question we find ourselves provided with scant knowledge that at the moment is capable of being applied practically. Experimental studies have shown clearly that recovery from the disease is effected by means of immunity principles that appear and persist for a long time—perhaps for years—within the blood. It has indeed been found possible in animals to apply the blood serum taken from recovered human beings and monkeys in such a way as to prevent the development of paralysis in monkeys following the inoculation of the virus (Flexner and Lewis). More recently still the fact has been ascertained that several larger domestic animals, including the horse, sheep, goat and pig, can be made to develop the immunity principles in their blood by subjecting them to injections of the spinal cord and brain of monkeys containing the living virus (Flexner and Clark). But these sera do not hold out any great hope of beneficial application in the treatment of developed poliomyelitis in human beings, for the reason that they are relatively weak in the immunity principles. An effort is therefore being made to approach the therapeutic problem through another avenue, namely, the employment of drugs. At the outset it is patent that since the drugs must come to act in the region of the central nervous system, the choice is restricted to those that beside possessing antiseptic properties can yet be applied to that sensitive part. We possess almost no drugs that exhibit the property of "internal antisepsis" so called, or in other words, are capable of exerting their antiseptic action in the interior of the body, in the presence of the proteins of the blood and tissues. Just here account should be taken of the pathogenesis of epidemic meningitis, since it is on it that the selection of the drug and the manner of its administration may come to be based. The evidence at hand points to the meninges as being the location of the primary lesion of the disease. It would seem as though the virus of poliomyelitis became first implanted on the leptomeninges, in which it developed, causing a

cellular exudation that affects especially the blood-vessels, the partial obstruction of which leads to the secondary production of the lesions of the nervous tissue itself. It is indeed not excluded that a direct action of the virus of poliomyelitis on the ganglion cells takes place, but this effect, if produced, appears to be less general and constant than the effects on the meninges. Hence the problem that presents itself is one that has to do with the control of the primary meningeal lesions, that in turn are caused by the virus present within the interstices of their tissues, as well as doubtless, at some stage of the process, within the cerebrospinal fluid itself. What is required then are antiseptic drugs having a special power to destroy this virus, and of very low toxicity, that can be made to exert their principal action on the meninges and in the subdural space. We possess in hexamethylenamin (urotropin) a drug which fulfils certain of these conditions. It is an internal antiseptic of some power, and is eliminated in some degree from the general circulation into the subdural space (Cushing and Crowe). On empirical grounds the drug has already been administered in cases of epidemic poliomyelitis, but whether with any definite effect is not known. Administered to monkeys prior to or coincident with inoculation and repeated daily afterward, hexamethylenamin is capable in some instances of preventing paralysis, and in others of lengthening materially the incubation period of the disease (Flexner and Clark). However, its powers in this direction are limited. On the other hand, its chemical composition is such as to permit of the addition of other chemical groups to the original molecule, in virtue of which the antiseptic power may be intensified. Through the employment of this means, a number of relatively non-toxic compounds have already been produced, which far exceed in internal antiseptic value the original drug, and some of these have already been applied experimentally with some degree of success to the prevention of the development of the paralysis following inoculation of the virus (Flexner, Jacobs and Clark). Whether any of these drugs will prove applicable to the treatment of human beings the victims of poliomyelitis it would be hazardous to predict, but it seems not improbable that some advance should be made along this line of investigation.

The case for the treatment of human beings is less hopeless, as I view it, than is commonly believed. It should be taken into account that much of the supposed damage inflicted on the nervous system of human beings at the onset of the paralysis is remediable. For the brunt of the disease falls not on the nervous tissue, but on the meninges, where it can in turn be opposed by therapeutic measures; and the severer nervous lesions are not in the most instances absolute, but they are merely relative and often probably merely functional in nature, since as many as 25 per cent. of the paralyzed may make complete recovery, and there is restored to a far larger percentage, by the usual processes of delayed resolution, a considerable degree of power in and use of muscles once severely paralyzed.

INFANTILE PARALYSIS

THE MOST PROMISING OUTLOOK FOR IMPROVEMENT IN TREATMENT FROM THE STANDPOINT OF THE PEDIATRICIAN

J. H. M. KNOX, JR., M.D.
BALTIMORE

GENERAL STATEMENTS

We now know that epidemic infantile paralysis is a result of an infective process produced by a specific virus which affects particularly the vessels of the meninges, leading to marked hyperemia, infiltration and inflammation, and to secondary involvement and degeneration of certain of the adjacent nerve-cells and fibers. The disease itself is a self-limited one, terminated by the production within the organism of antibodies to the specific virus. The duration of the acute symptoms may vary from several days to as many weeks, when they may end fatally or in complete recovery, or may be followed by the palsy of one or more muscles, dependent on the site and the extent of the nerve affection. The early paralysis is always of greater extent than the residual palsy, and is due apparently to pressure on nerve trunks by the edema and infiltration of the meninges. It is only after the disappearance of these acute phenomena that the extent of the lasting palsy due to nerve degeneration can be ascertained.

The *treatment* of the disease as presented to the pediatrician consists, in the first place, (a) in an attempt to lessen the severity of the attack, (b) in an effort to render the patient more comfortable during the course of symptoms, and (c) in the prevention of deformities, the result of disturbed muscular balance; and secondly, in averting the spread of the disease from the patient to others.

DIAGNOSIS

In regard to the effort to alter the course of the disease there are at present great difficulties. The diagnosis of the malady can rarely be made from the symptoms until the development of the paralysis. It usually begins with a febrile onset accompanied frequently with sore throat or digestive disturbances and more or less general hyperesthesia and sweating. These are rarely sufficient to distinguish it from other infectious ailments. However, in an epidemic the occurrence of these symptoms in a patient should lead certainly to the suspicion of poliomyelitis. The diagnosis can be considerably strengthened by an examination of the spinal fluid. Here there is an increase in the number of

cellular elements, particularly in the lymphocytes and in the protein contents of the fluid. The value of this aid in diagnosis was strikingly illustrated in a case reported by Dr. Frissell,[1] in which the symptoms of infection were present but physical examination otherwise negative. The condition of the spinal fluid sent to Dr. Flexner was found to resemble that seen in monkeys inoculated with the virus of the poliomyelitis, just before the onset of paralysis. By the same means the presence of meningitis, often difficult to distinguish clinically from certain forms of infantile palsy, can usually be excluded.

The laboratory may also be of assistance in the diagnosis of the disease by testing the sera of the suspected patient on monkeys; if the condition is poliomyelitis the blood-serum of the patient mixed with an active virus *in vitro* will neutralize it and the effect of the mixture when injected into a susceptible animal will be *nil*.[2]. This method would be particularly serviceable in the recognition of sporadic and unusual cases in their early stages.

The disease, then, being recognized or suspected, have we any means at hand to control its course? Certainly none that is specific or satisfactory. Active immunization by intracranial injections of the virus has been repeatedly carried out with success in susceptible monkeys,[2] but a sufficiently active curative serum to be of therapeutic value for human beings has not yet been obtained, although serum from immunized animals or from those recovered from the disease will protect a susceptible monkey when injected intraspinally twenty-four hours after the injection of the virus. More hopeful as a therapeutic agent is the administration of hexamethylenamin (urotropin). Cushing, Crowe, Morris and others have shown that after the admininstration of this drug formaldehyd quickly appears in the blood and secretions of the body, including the spinal fluid, and it is thought that this antiseptic may destroy the virus, or at least deter its action in the congested meningeal vessels and on the nerve-cells.

On the ultimate result of treatment with this drug and with closely related products it is too early to speak positively from clinical experience. The number of cases in which good results are reported from the use of hexamethylenamin in small doses by the mouth is constantly growing and there is considerable experimental evidence in its favor.[3]

Thus it was found at the Rockefeller Institute, when the active virus was injected intracerebrally into monkeys, to which hexamethylenamin had been given for some time, in a proportion of these animals the incubation period of the disease was prolonged and in some the paralysis was entirely prevented. The effect of hexamethylenamin is probably not

1. Jour. Am. Med. Assn., 1911, lvi, 661.
2. Jour. Am. Med. Assn., 1910, lv, 1105.
3. Jour. Am. Med. Assn., 1910, lv, 1804.

lasting and it gives no increased resistance to reinfection at a later period. It does, however, hold out some hope that if given before the paralysis begins this may be diminished, and it may be serviceable also in preventing the escape of the virus from the body.

TREATMENT

The duty of the physician to his patient is by no means completed in his rather unsatisfactory attempt to make a diagnosis and to lessen the severity of the malady. He can do much to make the child more comfortable. He is dealing with an infectious disease and one associated usually with more or less discomfort or pain. Complete *rest* is the first and most essential factor in the treatment of the disease. This must be secured, with an abundance of fresh air, preferably in the open.

The patient should be kept perfectly quiet and, better, completely isolated. The bowels should be opened and moved regularly and the diet should be light and nutritious as in other febrile conditions.

The suggestion of Lange[4] and Hohman[5] that the spinal column should be immobilized in a plaster cast will probably be serviceable in those cases in which the pain is particularly severe. Occasionally sedatives, best codein or morphin, may be necessary.

Cupping near the spinal column by the Bier method has many advocates, but it is doubtful whether intraspinal congestion can be relieved by this method.

A warm bath or pack with a cool application to the head may have a quieting effect in the early stages. The administration of nerve tonics, especially of strychnin, and of irritating procedures, such as electrical treatment or massage, must be carefully avoided at this time.

When the acute symptoms have subsided the patient enters the second stage of the illness, in which, although the fever has gone, there may be sensitiveness along the nerve trunks and on passive motion; there may be also contraction of the limbs due to pain which does not allow them to be brought into their normal positions. It is important that the absolute rest should be continued and that any over-stretching of paralyzed muscles, either from pressure of bed clothes or from gravity or from the pull of sound muscles should be prevented by the arrangement of sand bags, pillows, etc. At this time, heat as a moist or dry pack may relieve the tenderness.

The patient may be said to enter on the convalescent stage of the disease when the sensitiveness has disappeared and there are no contractions due to irritation. This stage lasts, as pointed out in the admirable report on infantile paralysis in Massachusetts in 1909, until all potential

4. Tr. Am. Pediat. Soc., 1910, xxii, 170.
5. München. med. Wchnschr., 1909, lvi, 2508.

power has been regained and until the deformities require no further attention. It is important to emphasize the fact, not sufficiently understood by the physician, that the muscle power returns continuously, though slowly, through months and even years, and during all this period repeated observations and treatment are indicated.

It should be the special endeavor at this time to prevent deformity and assist in the recovery of nerve and muscle power. The normal balance of the muscles about the joints should be maintained at all hazards, and the over-stretching of paralyzed muscles by the contraction of unaffected opposing muscles should be prevented. Judson[6] has emphasized the value of keeping the patient long in a recumbent position. He feels that the large predominance of the residual paralysis in the lower as compared to the upper extremity is due in part to the attempt of the patient to sustain his weight on the impaired muscles in the legs and feet. No corresponding exertion is demanded of the arms and hands. He suggests in many cases to extend the recumbent position so long as eighteen months.

The means at hand for stimulation of nerve and muscles are electricity, faradic when possible, and when response to this is lost, a galvanic current should be used; applications of various forms of heat, for the improvement of the circulation and the prevention of the comparatively low temperature of the paralyzed muscles, and massage, which improves the circulation and supplies artificial stimulus to both nerves and muscles. All these measures, however, are claimed by Sachs[7] and Strunsky[8] and others to be of much less value than what may be called *muscle training*. Strunsky in a recent article insists that the dominant element of success in the restoration of function is in *suggestion*, in securing the *cooperation* of the patient in the effort to make the desired movement, and that massage, passive motion and electricity, when helpful, are so because they are means of obtaining this end. "A bright child," he says, "one susceptible to impressions, makes better progress during the treatment than the stupid child." "Well directed massage may be the instrument that arouses the will power to concentrate to the utmost during muscular contraction, and leads to the building up of the mental and motor brain cells." An interesting contribution to this subject might be made on paralyzed monkeys and a comparison instituted between the prevention of atrophy or the restoration of function to muscles treated by electricity, by massage or by having such animals attempt voluntarily to make certain special movements. Microscopic examinations of such material might be instructive.

6. Denver Med. Times, Oct. 1, 1907.
7. Jour. Am. Med. Assn., 1910, lv, 48.
8. Am. Jour. Dis. Child., 1911, i, 266.

The surgical treatment of deformities resulting from infantile paralysis such as muscle and tendon transplantation and nerve grafting, or a discussion of the many effective mechanical devices for preventing and correcting deformities, does not fall within the scope of this paper. It remains only to refer briefly to the prevention of the spread of the disease from the patient to others.

Mention has already been made of the probable value of hexamethylenamin or similar germicidal drugs. It may be that the administration of this drug to those in attendance on a patient suffering from infantile paralysis may diminish their susceptibility to the disease. It should certainly be given to the patient during the acute stages, not merely for its possible effects on his infection, but because by this means the danger to those exposed may be lessened.

The studies at the Rockefeller Institute have shown that at least one portal of entry of the virus is in the nasopharynx and that the virulence of the virus is destroyed by the application of 1 per cent. hydrogen peroxid. It is rational, therefore, to apply this disinfectant to the nasopharynx of both patient and attendant at frequent intervals, and as Osgood and Lucas[9] have shown that the virus may persist for at least five months or longer in the nasopharynx of monkeys, this treatment of the patient should be continued, at perhaps longer intervals, for a more or less indefinite period.

804 Cathedral Street.

9. Jour. Am. Med. Assn., 1911, lvi, 495.

THE RÔLE OF MINERAL SALTS IN THE METABOLISM OF INFANTS *

B. RAYMOND HOOBLER, M.D.
NEW YORK

It is the purpose of this paper to present, in rather broad outlines, the part which mineral salts play in carrying on the physiologic functions of the body, and in what manner they contribute to the various pathologic processes to which the infant and young child are subjected.

This field of metabolic research has been the last to be undertaken, and just now we are coming to realize its vast importance, not only in connection with their own functions, but in connection with the influence they have on the metabolism of fat, protein and carbohydrate. The chief reason for having failed to realize the importance of the mineral salts in metabolism is that it has long been thought that the salts contributed in no way to the nourishment of the child. It has been only recently that they have taken their rightful place as indirect energy producers.

HISTORICAL

The first investigator to concern himself with the value of mineral salts was von Liebig,[1] who, as early as 1840, studied the action of mineral salts both in animal and vegetable life, and many of his early deductions have become firmly fixed as laws in the field of mineral salts metabolism. C. Voit[2] is another investigator whose work on the action of sodium chlorid, as early as 1860, first gave to that salt its prominence above all others in the human economy. Vierordt was also an indefatigable worker, and as early as 1877, from meager data then present, had calculated absolute and relative heat and estimated child's metabolism. J. Forster,[3] in 1873, added his convincing experiments on the necessity of the mineral salts to the continuance of life, and these were further reinforced by the work of Lunin[4] in 1881. As time advanced, the roster of those who worked in the field of mineral metabolism contains the names of many

---

*Read, by invitation, before the meeting of the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

*From the laboratories of the Presbyterian Hospital and Cornell University Medical College.

1. Von Liebig, J.: Chemie in ihrer Anwendung auf Agrikultur und Physiologie, 1876, p. 332.

2. Voit, C.: Ueber den Einfluss des Kochsalzes auf den Stoffwechsel, München, 1860.

3. Forster, J.: Ztschr. f. Biol., 1873, ix.

4. Lunin, N.: Ztschr. f. physiol. Chem., 1881, v.

notable investigators, as G. v. Bunge, Michel, Keller, Loeb, Muller, Schlossman, Blauberg, Rubner, Huebner, Freund, v. Noorden, and in these latter days the work is being carried on enthusiastically by L. Langstein, L. F. Meyer, E. Schloss, J. A. Schabad and others abroad, and by Howland, Schwartz, Talbot, Veeder, and others in this country.

A GENERAL VIEW

In undertaking a problem of this kind, it is well at the beginning to take a general view, first of the physiologic action of the mineral salts as a whole, and then to study what has been definitely determined as to the action and influence of each of the mineral constituents. Then by inquiring into the mineral constituents of the new-born and of older children, one will be in position to learn the mineral needs of the growing organism, and, knowing them, to ascertain how best to supply them, and to study the factors which enter into the proper utilization of the salts ingested in the food and to determine whether or not this utilization is sufficient to meet the demands of the growing infant.

First, then, a general view of the physiologic action of the mineral salts as a whole. Physiologists are generally agreed, and their findings confirmed by physiologic chemists, that the important functions of the mineral salts are as follows:

1. They maintain the osmotic pressure in tissue cells, blood, and body fluids; controlling the flow of water to and from tissues; any deviation from normal causing a shrinking or swelling of tissue cells.

2. They regulate the reaction of the blood and tissue fluids. A deviation from this reaction inhibits the action of the various ferments, delays chemical processes, and if such reaction suffers much variation, death results.

3. Their presence in tissues and fluids gives rise to irritability of muscle and excitability of nerve through the action of their respective *ions*. Through this function the rhythmical contractions of the heart are maintained.

4. They act as catalysts for a large series of chemical reactions which take place during the processes of absorption, retention, utilization, and form combinations with waste products of metabolism in order to effect their elimination; for example, they act as carriers of excess acid materials in oxidation processes.

5. They share in the upbuilding and growth of the body, since they are a constituent of every cell; particularly do they take part in the changes which go on in the albumin bodies as they become intimately bound with the body proteins.

6. Their function in the intermediary metabolism of the ductless glands is very apparent from the large quantities of mineral salts found in these glandular organs.

7. Through a most excellent self-regulation, they protect against the acid poisons which the body is constantly producing.

8. Through the work of the various *ions*, electrically charged, some positively, some negatively, many important functions are being assigned to them, such as controlling body-weight, temperature, regulating the pulse, increasing leukocytes, etc. These and many more functions, not clearly defined, depend on the presence of the mineral salts in the body, and not on their presence alone, but their presence in definite relationships to one another.

ABSOLUTE NECESSITY OF SALTS

While physiologists have been busy defining the various functions of salts, other investigators have determined the absolute necessity to the maintenance of life of a certain quantity of mineral salts, and not only a certain quantity, but they have found that these salts must be in certain organic combination, as the following experiments will show:

Forster,[3] in 1873, fed pigeons on approximately ash-free diet, and found their bones brittle, and they all died within a month. He also fed dogs on salt-poor diet, and they lived from twenty-six to thirty-six days.

Lunin[4] showed by his classic experiment that the salts must be in organic combination to be available. He found that mice thrived well on dried whole milk, but that if the salts were extracted from the milk, and they were fed only the protein, fat and carbohydrate, they shortly died, and further, after abstracting the salts, if he substituted the same quantity of other mineral salts, adding them to the protein, fat and carbohydrate, the mice died. Furthermore, mice fed on ash-free food, plus sufficient sodium carbonate to take the place of the usual salts, lived twice as long as mice fed only on ash-free diet; nevertheless, they succumbed, demonstrating that even with the necessary amount of bases carbonates cannot supply the salt needed.

Rohmann[5] added further confirmation to the value of salts. He fed mice a mixture of simple organic and inorganic food-stuffs. These mice lived and were able to produce young, but the latter could not be raised on artificial food, nor could they be made to produce living young.

It is evident from this latter experiment that artificial foods may be sufficient for the adult, whose supply of minerals is well established, but it is not sufficient to produce healthy offspring.

Abderhalden[6] believes that the same physiologic importance of salts exists for the animal kingdom as has been shown by von Liebig and others to exist for the vegetable kingdom.

The salts have a very important bearing on the absorption and retention of other food constituents, e. g., in a large nitrogen retention there is usually a large ash retention, and when ash is eliminated in large quantities there is usually an accompanying loss of nitrogen.

T. B. Robertson[7] points out how intimately the precipitation and coagulation of protein depends on the salts present in the solution as *ions*. Indeed it is becoming more and more to be appreciated that the various food constituents have a very intimate influence, the one on the other, and it is along this particular line that metabolism studies are directing themselves.

Recognizing, then, that the mineral salts are necessary to life, let us inquire what salts, and in what proportion in the body, Nature has stored

---

5. Rohmann: Klin.-therap. Wchnschr., 1902, No. 40.
6. Abderhalden: Physiological Chemistry, p. 356.
7. Robertson, T. B.: Jour. Biol. Chem., May, 1911.

them, by the action of which not only life is maintained, but energy developed and growth permitted. We are indebted to a number of investigators for information on the ash-content of the human organism both during fetal life and later.

Fehling[8] gives us the following figures of the ash-content at different periods of fetal life:

Period of Life.	Ash Content; Per Cent. of Total Weight.
Fetus, 6 weeks	.001
Fetus, 4 months	.98
Fetus, 5th month, first half	1.4
Fetus, 5th month, second half	1.43
Fetus, 6th month	1.94
Fetus, 7th month	2.94
Fetus, 8th month	2.82
Fetus, 9th month	3.3
In the new-born	2.7
In the adult	4.4

It will be noted, therefore, that from the earliest observation of fetal life to those on adult bodies, there is a gradual increase of the ash-content. This increase is most rapid in terms of percentage of body weight during the fetal period, and thereafter the increase is much slower.

Let us now ask ourselves the question as to the mineral constituents contained in the total ash-content and study their relative amounts. Hugounencq[9] has given us this information for fetal life, and Soldner[10] for the new-born. Soldner found that there was 75 gm. of ash in a new-born child which was equal to 2.7 per cent. of its body weight, or 9.4 per cent. of the dry residue.

	Total Ash in Parts Per 100							
Period of Life.	Cl	P_2O_5	SO_3	CaO	MgO	K_2O	Na_2O	Fe_2O_3
Fetus, 5 months	8.59	34.36	1.8	32.5	1.58	8.28	12.62	.4
Fetus, 6 months	7.75	34.94	1.78	34.6	....	7.21	10.62	.39
Fetus, 7 months	8.53	35.39	1.46	34.13	1.17	8.45	10.95	.398
New-born (Soldner), average of 6	6.61	.....	2.02	38.08	1.43	7.06	7.67	.83

Soldner, arguing from the average ash content of six new-born infants, concluded that there was a daily need of 1.4 gm. of mineral ash, and an infant should retain of the intake, chlorin 14 per cent., potassium 11 per cent., sodium 35 per cent., CaO, MgO and P_2O_5 at least 65 per cent. of the intake.

It will be noted that phosphorus and calcium make up considerably over half; sodium about an eighth, and potassium and chlorin about a twelfth of the total ash-content, and that sulphur, magnesium and iron make up but a small part of the total.

8. Fehling: Cited by Freund, in Pfaundler and Schlossman, i, 363.
9. Hugounencq: Compt. rend. Soc. de biol., li, 537.
10. Camerer and Soldner: Ztschr. f. Biol., 1900-3, xxxix, xl, xliii, and xliv.

Bunge,[11] after a careful study of the mineral contents of the milk of lower animals and estimating the daily requirements of their offspring, attempted to show that the ash-content of the body was in correct proportion to the ash-content of the various animals. But when this was applied to the nursing infant his analogy failed, and the problem did not solve itself as readily as this hypothesis would indicate. It is evident that the main metallic elements are calcium, sodium, potassium and magnesium; the main acid salts being phosphoric, hydrochloric, carbonic and sulphuric, calcium phosphate being the most abundant of all the salts.

It should be further noted that the phosphorus and calcium content of the body increases in percentage, and that the other elements remain at the same or less percentage, but of course their absolute amount gradually increases.

The difference between the ash-content of a new-born and the ash-content of a 4-months' old child represents the change which must take place in the mineral salt storing. In actual figures the child must add to his weight, during the first four months, the following quantities of the various minerals:

	Gm.
K_2O	2.0
Na_2O	2.57
CaO	11.75
MgO	.31
Fe_2O_3	....
P_2O_5	10.48
Cl	1.12
S	....

It will be noted what really small quantities of the mineral salts are added to the body—extremely small when we consider the large quantity which a child during the first year must ingest. It is estimated that only about 4 per cent. of intake goes to growth in early months and later only half that amount. It is evident that a large quantity must be worked over. Taking mother's milk as a basis, during the first twelve months of life there is approximately 800 gm. of total ash ingested. This is divided among the various mineral salts as follows:

	Gm.
K_2O	276.
Na_2O	19.6
CaO	157.6
MgO	27.2
Fe_2O_3	8.0
P_2O_5	117.6
Cl	117.6
SO_3	57.4
Total	791.0

If we take cow's milk as a basis, the picture is entirely different. Taking the average amount fed as outlined in Dr. Holt's text-book, an

11. Bunge: Cited by Freund, Pfaundler and Schlossman, Vol. i.

infant would ingest approximately 1,500 gm. of total ash during the first year of life, which would be divided among the various mineral constituents as follows:

	Gm.
K_2O	377.0
Na_2O	93.0
CaO	344.0
MgO	41.0
Fe_2O_3	4.2
P_2O_5	487.4
Cl	84.0
S	69.4
Total	1,500.0

This naturally leads us to a two-fold conception of the use which the body makes of the salts. First, a certain small per cent. is firmly bound with the tissues of the body and only escapes when such tissues are destroyed in oxidation; and a second group which are simply held in solution in the body fluids ready to be excreted, or to act as bases or alkalies to take up the products of cell destruction, or combine with acids set free in the processes of catabolism, or in the form of *ions* to subserve definite physiologic functions. It should be borne in mind that only a small part of the mineral salt intake in any day's feeding is added as an integral part of the tissue, and that by far the largest part is simply held in solution awaiting its excretion, either through the skin, urine or back into the intestinal canal. With sulphur and phosphorus the problem is a little more complicated, as these two substances are in exceedingly close chemical relationship with albumin, and before they can be set free the foreign albumin molecule must be torn down before it can be again rebuilded into the tissue substance and fluids of the host.

Having noted just what minerals and acids are present in the body at the end of fetal life, it behooves us to inquire into the method by which we can continue to supply the needs of the infant as relates to its mineral constituents so as best to foster its normal growth and aid in supplying its daily energy requirement. Nature has supplied us with a most excellent criterion by which we may reach a solution of this problem, viz., in normal mother's milk. Let us, therefore, address ourselves to a study of Nature's method of supplying the need of the growing infant by carefully considering the mineral constituents and their relative proportions in mother's milk.

In early mother's milk, i. e., colostrum, according to Camerer,[12] we have a marked increase from the first to the seventh day in the ash-content as follows:

Day after delivery	1	2	3	4	5	6	7
Ash content in per cents	0.1	0.5	0.7	0.9	1.0	1.1	1.3

12. Camerer: Cited by Freund in Pfaundler and Schlossman, i, 386.

Thus Nature provides in the early nursing period for a very rapid increase in the mineral constituents of the food. In mother's milk there is about 2.0 gm. of total ash to 1,000 gm. of milk. This 2 gm. of ash is divided among the various mineral constituents according to various authors, as follows:

In 1,000 gm. of mother's milk, there is, according to

	Bunge 1[15] Gm.	Bunge 2[15] Gm.	Camerer[13] and Soldner Gm.	Blauberg[14] Gm.
K_2O	0.780	0.703	0.884	0.69
Na_2O	0.232	0.257	0.357	0.049
CaO	0.328	0.343	0.378	0.394
MgO	0.064	0.065	0.053	0.068
Fe_2O_3	0.004	0.006	0.002	0.02
P_2O_5	0.473	0.469	0.310	0.294
Cl	0.438	0.445	0.591	0.294
SO_3	....	.....	.....	0.143

The ash-content of mother's milk does not remain constant, as is shown by Soldner[16] in his examinations of mother's milk on the eighth and seventieth days. In 1,000 gm. of mother's milk on the eighth day, there was 3 gm. of total ash, and in the same quantity on the seventieth day there was 2 gm. of total ash divided as follows:

	Eighth day Gm.	Seventieth day Gm.
K_2O	1.008	.259
Na_2O	.448	.176
CaO	.376	.381
MgO	.054	.052
Fe_2O_3	.0022	.00125
P_2O_5	.320	.288
SO_3	.096	.063
Cl	.716	.342

From the above, it would seem that the fixed alkalies K and Na diminish greatly as does also the chlorin content of the milk, while the bone-forming constituents, viz., calcium, phosphorus and magnesium, remain nearly constant. In cow's milk the relations are entirely different as is shown by the exceedingly large ash-content of 7.8 gm. per 1,000 gm. of milk as against 2 gm. in 1,000 gm. of mother's milk. Not only does cow's milk contain more ash, but in vastly different proportion of mineral constituents than mother's milk, as will be seen by the following table when compared with the preceding table showing mineral contents of the ash of mother's milk. In 1,000 gm. of cow's milk there is:

13. Camerer and Soldner: Cited by Albu-Neuberg, Mineralstoffwechsel, p. 51.

14. Blauberg: Cited by Langstein and Meyer Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, page 15.

15. Bunge: Cited by Albu-Neuberg, Mineralstoffwechsel, p. 51.

16. Soldner: Cited by Freund, in Pfaundler and Schlossman, p. 377.

	Bunge[15] Gm.	Soldner[17] Gm.	Hoobler Gm.	Soldner[17] Gm.
K_2O	1.766	1.720	.....	1.885
Na_2O	1.110	0.51	.....	0.465
CaO	1.599	1.980	1.600	1.72
MgO	0.210	0.20	0.167	0.205
Fe_2O_3	0.004	.....	.....	0.021
P_2O_5	1.974	1.82	2.140	2.437
Cl	1.697	0.98	1.86 (NaCl)	0.820
S	....	.....	0.33638	....

It will be seen that in the same quantities of milk, that of the cow contains over twice as much potassium, five times as much sodium, phosphorus and calcium, four times as much magnesium and chlorin and six times as much sulphur. And, further, these salts are not in the same organic combination in one as in the other, as shown by Keller,[18] and also by Schlossman,[19] as relates to phosphorus, and when we consider that it is the organically bound salts only, as shown by Lunin,[4] which are available, this factor is a very important one.

Not only are the salts organically bound, but there is a peculiar specificity about the whey containing the salts of mother's milk. Meyer[20] has shown that not only the protein and fat of mother's milk, but even the casein and fat of cow's milk, are well absorbed and retained when mixed with the whey of mother's milk. Children fed on the fat and protein of mother's milk mixed with the whey of cow's milk are not able to utilize these food products and do badly. It would seem that some constituent in mother's milk whey contains the essential dynamic force for making the casein and fat of both mother's and cow's milk available for nutritive purposes.

Having now considered separately the salts of the child's body and the salts of the two most common foods, let us study the processes which take place when these foods are ingested by the infant. It would contribute to a continuity of thought if we were to follow each individual salt through its various metabolic steps under perfectly normal conditions and discuss them under the heads of ingestion, absorption, retention and elimination, considering the results obtained by investigators in the use of mother's milk and cow's milk.

After having considered these steps in normal metabolism, I shall address myself briefly to abnormal conditions of metabolism, desiring rather to give most attention to the consideration of the normal. I shall take occasion to consider, along with the findings of literature, some results obtained by me in a series of metabolism studies which I have

17. Soldner: Cited by Langstein and Meyer, Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, page 15.

18. Keller, A.: Arch. f. Kinderh., 1900, xxix.

19. Schlossman: Arch. f. Kinderh., 1905, xl.

20. Meyer, L. F.: Cited by Meara, Problems of Nutrition in Early Life, Arch. Pediat., xxvii, 401.

TOTAL ASH

Food	Intake	Elimination: Feces	Elimination: Urine	Absorption: Gm.	Absorption: Percent.	Absorption: Per Kilo	Retention: Gm.	Retention: Percent. of Intake	Retention: Per Kilo
Mother's milk (Blauberg)	1.13	0.193	0.373	0.937	82.9	....	0.56	49.5	....
Mother's milk (Blauberg)	1.32	0.24	0.47	1.08	81.8	....	0.61	45.9	....
Cow's milk (Soldner)	6.841	2.686	3.1341	4.15	60.7	....	1.013	14.8	....
Diluted cow's milk, 2.1% fat (Hoobler)	8.9691	4.2651	4.7966	4.7039	53.0	.565	.....	....	....
Cow's milk, 4% fat (Hoobler)	9.4808	3.1390	3.0834	6.3418	66.8	.808	2.8917	43.5	.368
Cow's milk and cream, 5.4% fat (Hoobler)	8.7634	1.8675	4.1493	6.8959	78.6	.861	2.7465	37.8	.344
Cow's milk (Blauberg)	6.84	2.68	3.13	4.15	60.7	....	1.01	14.8	....

Figures given above are in grams in 24 hours.

carried out in the wards and laboratory of the Presbyterian Hospital on a perfectly healthy infant of 9 months who had been fed on cow's milk from the time of his birth, details of the experiment, as relates to nitrogen metabolism, having already been published.[22]

TOTAL ASH

I will first consider the figures covering the entire mineral metabolism as represented by total ash, and will then discuss its various phases.

INGESTION

First let us consider the intake. It should be remembered that mother's milk is relatively poor in ash-content while that of cow's milk is exceedingly rich, so that one is not surprised to note that the intake of total ash through breast feeding is very much less than with cow's milk feeding. From the figures of Blauberg, Soldner, and my own determinations, the ash intake in artificially fed children is from six to nine times greater than that of breast-fed children.

ABSORPTION OF TOTAL ASH

Various observers have recorded their findings of ash absorption in mother's milk, varying from 81.82 per cent. by Blauberg to 53 per cent. of intake by Schlossman; Biedert's determination was 77 per cent., and that of Rubner and Heubner 79.42 per cent., while the absorption of total ash of cow's milk by different authors is as follows (see also p. 115):

	Per cent.		Per cent.
Soldner	60.7	Biedert	65.1
Schlossman	70.	Hoobler	53.
Tangl	62.1	Hoobler	66.8
Blauberg	53.72	Hoobler	78.6

It will be seen that the absorption per cent. is 15 per cent. to 25 per cent. better on mother's milk, but because of the large intake the actual amount absorbed is very much larger in cow's milk feedings than in breast-fed. For example, 1.08 gm. was absorbed in twenty-four hours on mother's milk, while on cow's milk from 4 to 6 gm. were absorbed daily. Thus approximately four to six times more is absorbed in artificial feeding.

As we shall see later, this better absorption of mother's milk ash lies in the fact that calcium, magnesium and phosphorus are much better absorbed. As was demonstrated in my work on the various fat feedings, and now being published in the Presbyterian Hospital Report of this year, nitrogen, chlorin, sulphur and magnesium were absorbed in the same ratio as these elements existed in the food. The greatest variations from the ratio in the food occurred in calcium and phosphorus.

22. Hoobler: Arch. Pediat., 1910, xxvii, 853.

RETENTION

Without doubt the best criterion of availability and utilization of any given food-stuff is not its large per cent. of absorption, or even its large absolute amount of absorption; but rather the absolute amount retained. Literature does not yet contain reports which cover sufficient periods of investigation to feel quite sure that these so-called absolute retentions are permanent or simply transitory, since it takes weeks to utilize and eliminate the mineral salts. Therefore a prescribed diet should be carried out for weeks instead of days for most accurate results. However, the reports in literature show that the ash of mother's milk is well retained and this is but natural, for the salts come to the infant in much better form for utilization than in cow's milk.

In Blauberg's case on mother's milk (see total ash tabulation), the absolute retention was 0.61 gm., being 45.9 per cent. of the intake. In cow's milk feeding, the per cent. of retention is lower but the absolute amount is higher, owing to the much richer ash-content of the cow's milk. Blauberg's case on cow's milk feeding, having a retention of 14.8 per cent. of intake, represented an absolute amount of 1.013, being nearly twice the amount retained under mother's milk feeding. In my 9-month child there was retained 2.89 gm. or 43.5 per cent. intake. Blauberg found that with mother's milk feeding all the minerals were retained with the exception of sodium; in cow's milk there was a loss in Cl, S, and Na. It would seem that each child is a law unto itself so far as retention of mineral ash is concerned. It apparently takes it on just in accordance with the demands of physiologic growth.

In my determinations in connection with various strengths of fat in foods, I found that as compared with nitrogen retention, the retention of the mineral salts was relatively poorer. This poor retention was most marked on the lower fat food, better on the medium fat diet, and best as regards the absolute amount retained on the high (5.4 per cent.) fat diet. Retention of the salts in proportion to nitrogen was never in the same proportion as existed between the salts and nitrogen of the food.

ELIMINATION

The elimination through the feces and urine differs in amounts on mother's and cow's milk. In mother's milk feeding, one-third of the salts are eliminated through the feces and two-thirds through the urine, while in cow's milk feeding about half is eliminated by the urine and half by the feces, though the figures of different investigators vary. In my own figures the ash of the feces was three times as large on a 2.1 per cent. fat mixture as on a 5.4 per cent. mixture.

THE ANOMALIES IN THE METABOLISM OF TOTAL ASH

In the elaboration of Finkelstein's theory of food disturbances in infants and children, L. F. Meyer[23] has attributed to the mineral salts certain deleterious influences.

In each of Finkelstein's four stages of nutritional disturbance, Meyer finds that there is some anomaly in the salt metabolism. In the stage of *"Bilanzstörung,"* there is decreased retention of the alkaline earths. There is also a lessened retention of other salts.

In the stage of dyspepsia, the salt elimination by the feces is increased but the ash balance is not markedly changed. In the stage of decomposition the entire picture is determined by the loss of the mineral salts, particularly through the loss of the fixed alkalies. Through the fatty acids in the stools, the Ca and Mg are used up. The diarrheal stools of this period are due largely to alkali loss. The condition of relative acidosis of Steinits (and of alkalipenia of Pfaundler) takes place during this stage, due to the loss of alkali.

In the fourth stage, of intoxication, the salt metabolism is little known. There is a negative balance of chlorin and probably of the other mineral constituents. Whether the salt loss controls the water loss or vice versa is still a question, but since the urine is much decreased and the output of water by the feces is increased, it would seem that the salts were accountable for this diversion of the water elimination. It is evident that salts play an important part in every digestive disturbance of the infant and young child.

CALCIUM

The calcium need of the growing infant is well met through the abundance of its salts in the milk, either of mother's or of cow's. Calcium makes up one-fifth of the ash of mother's as well as of the ash of cow's milk. Calcium is taken into the body in organic and inorganic form. The organic combination is present in milk, yolk of eggs and vegetables, and the inorganic form in water used as a diluent and for drinking.

The importance of the calcium salts in the developing organism can hardly be overestimated. Physiologists[24] have shown that the calcium *ions* in the blood, though in small quantity, are yet absolutely necessary to the irritability of muscle. If calcium is present in too large quantities, as compared with Na and K *ions*, there is produced a tonic contraction known as calcium rigor.

Calcium has a definite specific action of its own and cannot be replaced by other earthy bases, as magnesium and strontium, as stated by Stewart.[25] The fact is well known that calcium is necessary to ferment action

23. Langstein and Meyer: Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, pp. 111-166.
24. Howell: Physiology, Ed. 2, 1907.
25. Stewart: Physiology, Ed. 1910, p. 542.

as shown by the coagulation of blood and the precipitation of casein in milk. Calcium is much the largest mineral constituent of the body. Its most common salt is calcium phosphate, which makes up a large part of the bone salts.

Jacques Loeb[26] has shown the necessity of calcium salts for the development of the lower forms of life, and Blauberg has shown that children who cannot metabolize calcium cannot survive.

Mother's milk contains only about 20 per cent. as much calcium as cow's milk; therefore we would expect a considerable variation in its absorption and retention, as is shown by the following:

CALCIUM AS CaO

The calcium of mother's milk is 0.394 grams in 1,000 gm. I found calcium of cow's milk to be 1.6 grams in 1,000 gm., or nearly four times as much in cow's as in mother's milk. (See also tabulation page 120.)

It will be noted first that the calcium intake in cow's milk feeding is about eight times greater than in mother's milk; that the amount actually absorbed and retained is four times greater on cow's milk than on mother's milk. However, a much larger percentage of mother's milk calcium is retained. It is evident, therefore, that the calcium of mother's milk is much better metabolized than the calcium of cow's milk, and since a healthy nursing infant shows no signs of a deficiency of calcium, we may well consider the amount which it gets as being the true calcium need. The absorption of calcium depends in part on the presence of accompanying salts; for example, if much alkali bases are present in the intake the absorption is diminished, whereas NaCl assists in calcium absorption. Calcium is more readily absorbed on flesh than on a vegetable diet.

ELIMINATION

It should be noted that the elimination of calcium is almost entirely through the feces; only 5 to 10 per cent. of the intake appears in the urine. This does not mean that the calcium is not well absorbed, but that it is excreted into the large intestine, as is proved by the fact that larger quantities of calcium are found in the large intestine than in the small intestine. It was Voit[27] who showed that 0.15 gm. of calcium per day was excreted from the inner surface of the intestine.

The amount of calcium excreted in the urine of infants fed on breast and cow's milk does not vary greatly, but the amount which appears in the feces varies greatly, being in some instances twenty times greater. Calcium makes up a quarter or a third part of the dried feces of cow's-milk-fed children, as against a much smaller portion in breast-fed. The

26. Loeb, J.: Cited by Meyer, Jahrb. f. Kinderh., lxxi, 1.
27. Voit: Cited by Howell, Physiology, Ed. 2, p. 834.

CALCIUM AS CaO

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk (Blauberg)	0.2884	0.0952	0.0127	.....	....	....	0.176	62.4	....
Mother's milk (Blauberg 5 mos.)	0.2720	0.0660	0.0310	0.2060	75.8	....	0.175	64.5	.026
Cow's milk (R. & H. 7½)	2.0824	1.142	0.0166	0.9370	45.1	....	0.924	44.4	.122
Diluted cow's, 2.1% fat (Hoobler)	2.0536	2.2687	0.0301	Negative	....	....	Negative	....	....
Cow's whole milk, 4% fat	2.0500	1.6962	0.305	0.3538	17.2	.045	0.3233	15.7	.041
Cow's milk and cream, 5.4% fat	2.0923	0.9515	0.0085	1.1408	54.5	.142	1.1322	54.1	.142

Figures given above are in grams in 24 hours.

form in which the calcium usually appears in the feces is that of the insoluble soaps, or in the form of calcium phosphate.

In my series of studies the elimination of calcium in the feces was greater on milk of lower fat content. As fat was increased in the food, the calcium was diminished in the feces. The calcium eliminated in the urine appears along with magnesium, bound with phosphoric, carbonic and uric acids. Iron is another mineral constituent which is excreted very poorly through the urine, and this leads one to group these two constituents together and to inquire if there are other characteristics. It should be noted that their presence in many organs, for example the thyroid gland, the liver, the spleen and the ovaries, suggests physiologic and chemical affinities as pointed out by Albu and Neuberg.[28] The internal secretions which play such a part in intermediary metabolism of the mineral salts, may be largely affected by the relationship of these two minerals. Calcium and phosphorus are closely allied in the bones, in the ovaries, and in the thyroid gland.

THE ANOMALIES OF CALCIUM METABOLISM

As a rule there is a great individual difference in the amount of calcium absorbed, and a further difference in the ability to retain the calcium absorbed. Rarely is such a condition due to the lack of calcium in the food, although many artificial foods are very poor in calcium. A diet containing less than 1 to 1.5 gm. CaO daily should be considered calcium-poor, except when on mother's milk feeding.

It has been shown that when calcium is purposely withheld from the diet of young puppies, rachitis develops, and the bones of young pigeons fed on calcium-poor diet are very fragile (Forster[3]). In the bones, in rachitis the mineral constituents are depleted, particularly calcium and phosphorus. The total ash of bones which normally is 65 per cent. falls to as low as 25 per cent. and the main loss falls on the calcium phosphate. The calcium loss in rachitis is largely through the intestine, with but little change in urinary calcium. In feces of rachitis, there is an increased elimination over that of healthy children, as shown by J. A. Schabad.[29] In rachitis particularly the weak point in the metabolism cycle may be the inability of the bones themselves to take up and build into bony tissue the calcium and phosphorus brought to them by the fluids, as has been pointed out by Albu and Neuberg.[28] The fact that calcium has much to do with the function of the nervous system has been shown by the calcium disturbances in tetany, as demonstrated by Schabad.[30] Further, the large proportional content of the brain tissue of the new-born in calcium

28. Albu-Neuberg: Mineralstoffwechsel, Berlin, 1906, p. 70.

29. Schabad, J. A.: Arch. f. Kinderh., liii, 241.

30. Schabad, J. A.: Monatschr. f. Kinderh., ix, No. 1; Jahrb. f. Kinderh., l, No. 1.

(0.168 per cent. CaO), as compared with an 8-year-old child's brain (0.05 per cent.) speaks further confirmation of this. There is a very appreciable loss of calcium from the nerve structures during the first year of life. Quest[31] found less calcium in the brains of children who died of tetany than of children of the same age without tetany.

Schloss[32] has more recently shown that subnormal body temperature in some cases depends on the presence of calcium *ions*. In the symptom-complex which Finkelstein calls *Ernährungstörung*, during the stage of *Bilanzstörung*, Meyer[23] has shown that there is a decreased retention of calcium due in part to the fact that the fats of the stools are increased, and these demand the alkaline earth to neutralize the fatty acids. There may be such a demand that not only will no calcium and magnesium be retained, but there may be an actual withdrawal of these salts from the body. This may account for a portion of the loss of weight in this stage of food disturbance.

IRON

Cow's milk and mother's milk contain about the same amounts of iron. Each is very poor in iron, and were it not for the relatively large amount stored in the liver and blood of the new-born there would be a deficiency in the early months of feeding. The following table shows that the form in which the iron is present has a large bearing on its availability. The iron of goat's milk is poorly absorbed and poorly retained, while the iron of mother's milk is well absorbed and well retained. Iron is eliminated almost entirely through the feces but a very small quantity through the urine.

Iron plays an important part in metabolism. It is specially important in the formation of the hemoglobin molecule. It acts as a catalyst in oxidation processes, especially in the group of nucleoproteins, as has been shown by Spitzer[44] and by Manchot.[45] Iron is presented for consumption in both the organic and inorganic form. The organic forms occur in the nucleoalbumins, in milk, yolk of eggs and in many vegetables.

IRON AS Fe_2O_3

In 1,000 gm. mother's milk, .02 gm. to .04 gm.
In 1,000 gm. cow's milk, .021 gm. (Abderhalden).

		Elimination		Absorption		Retention	
Food	Intake	Feces	Urine	Gm.	%	Gm.	%
Mother's milk	.00705	.00084	.00055	.00621	88.09	.00566	82.28
Goats' milk	.00344	.00259	.00009	.00085	24.71	.00076	22.09

Figures given above are in grams in 24 hours.

31. Quest: Cited by Freund, in Pfaundler and Schlossman, i, p. 285.

32. Schloss: Cited by Langstein and Meyer, Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, p. 21.

44. Spitzer: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 151.

45. Manchot: Cited by Albu and Neuberg, Mineralstoffwechsel, p. 151.

Magnesium as MgO

In 1,000 gm. mothers' milk there is 0.068 gm. MgO.
In 1,000 gm. cows' milk there is .205 gm. MgO.

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk (Blauberg)	0.047	0.0157	0.014	.....	....	....	0.0175	37.2	....
Cow's milk (Soldner)	0.15017	0.0944	0.03718	. ....	....	....	0.017	11.5	....
Diluted cow's milk, 2.1% fat (Hoobler)	0.10843	0.0058	0.0134	.10258	94.6	.123	0.0891	82.1	.011
Whole cow's milk, 4% fat (Hoobler)	0.07755	0.0300	0.04861	.04746	61.3	.045	Negative	....	....
Cow's milk and cream, 5.4% fat (Hoobler)	0.14999	0.0828	0.01909	.06719	44.7	.008	0.04809	32.0	.006

Figures given above are in grams in 24 hours.

MAGNESIUM

Magnesium and calcium are very closely connected in the metabolic function. They occur in the organism in much the same places and as salts of the same acids. Their proportion is CaO:MgO::40:1. Magnesium has a little wider distribution in the body tissues than does calcium. The latter occurs almost entirely—at least 99 per cent.—in the bones, while magnesium is found in muscle-tissue as high as 0.04 per cent. The part which magnesium plays in bone structure is important. Magnesium makes up about 10 to 15 per cent. of the total ash of bone. The relation of magnesium in these structures is about 1:9. The magnesium table on page 123 indicates that the Mg need of the growing infant on mother's milk is 0.047. Bunge, as cited by Albu and Neuberg, gives the magnesium need as 0.6. This seems rather high, for, since there is about 0.06 gm. Mg in a litre of mother's milk, it would require 10 litres to satisfy this need. Blauberg's breast-fed infant got but 0.047 gm. daily. The intake when fed on cow's milk varied; according to Soldner the daily intake was 0.15 gm., while my determinations showed intake varying from 0.07 to 0.15.

ABSORPTION

The absorption of magnesium which takes place through the small intestine is relatively very good. My determinations gave 94.6 as the per cent. of intake which was absorbed when feedings were low in fat. As the fat content of the food was increased, there was relatively poorer absorption, the percentages being 61.3 on a 4 per cent., and 44.7 on 5.4 per cent. fat mixture.

RETENTION

The retention of magnesium in my series was better on 2.1 per cent. fat mixture than on the 5.4 per cent. mixture. This retention varied inversely with the calcium retention so far as the amount of the fat in the food is concerned. In my findings for calcium, retention was poorest on lower fat mixtures and improved on the higher fat mixtures.

ELIMINATION

Excretion occurs both through urine and feces. On mother's milk in Blauberg's case, the excretion through either channel was about the same, while in cow's milk in some instances it was higher in urine and in others it was higher in the feces. In any event, the excretion is very small and that through the urine occurs as triple phosphates.

ANOMALIES OF RETENTION

There is more or less relation between Ca and Mg in the formation of oxalic acid concretions. It has been found that if the ratio of CaO to MgO be as 1 to 0.8 the concretion may be kept in solution. The smaller

Phosphorus as P_2O_5

	Total Gm.	Organically Bound, Gm.
In 1,000 gm. mother's milk	.294	42.3
In 1,000 gm. cow's milk	2.437	46.
In 1,000 gm. cow's milk (Hoobler)	2.140	....

Food	Intake	Elimination: Feces	Elimination: Urine	Absorption: Gm.	Absorption: Percent.	Absorption: Per Kilo	Retention: Gm.	Retention: Percent.	Retention: Per Kilo
Mother's milk	0.2768	0.0363	0.0481	.....	....	....	.192	69.13	.....
Mother's milk, 5 mos.	0.2030	0.0220	0.088	0.1810	89.1	....	.093	45.9	.0138
Cow's milk	1.4429	0.5352	0.5003	.....	....	....	.4074	30.7	.....
Cow's milk (Keller's 2¾ mo)	0.8248	0.1073	0.4106	0.7174	87.1	....	.3068	37.2	.0626
Cow's milk (Blauberg's 7½ mos.)	2.0605	0.9627	0.5899	1.098	53.28	....	.5079	24.2	.0671
Diluted cow's milk, 2.1% fat (Hoobler)	2.2155	0.7648	1.152	1.4507	67.0	.174	.3320	14.5	.040
Cow's milk, whole, 4% fat (Hoobler)	2.7418	0.59914	2.009	2.1426	78.1	.274	.1336	4.8	.0171
Cow's milk and cream, 5.4% fat (Hoobler)	2.2346	0.3789	1.336	1.8556	83.0	.235	.6196	27.7	.0657

Figures given above are in grams in 24 hours.

the calcium and the larger the Mg content the easier becomes the solution of calcium oxalate.

PHOSPHORUS

Of all the mineral elements, perhaps none has been studied more assiduously than phosphorus. Phosphorus is brought into the body in two very different forms, viz., that which is organically bound, occurring in milk, eggs and legumes, and a small part as phosphoric acid. When in organic combination it is found as nucleoalbumin, nuclein, vitellin, casein and lecithin.

The source in which we are most interested is that of mother's and cow's milk, and these two foods differ considerably in the amount of organically bound phosphorus. Mother's milk contains 0.31 to 0.45 gm. per liter of P_2O_5, while cow's milk contains 1.81 gm. P_2O_5 per liter. Keller[33] has shown that of the phosphorus of mother's milk 77 per cent. is organically bound, while in cow's milk only 27.9 per cent. is so bound. Of this organically bound phosphorus 54 per cent. occurs as nucleophosphorus in mother's milk, and but 13.4 per cent. in cow's milk, so that it is very evident that the phosphorus of cow's milk, though larger in actual quantity, is not in such form as to be available, as is the case of mother's milk. The nucleins of milk make up 41.5 per cent. of the total phosphorus of mother's milk, while of cow's milk only 6 per cent. is in that form. In mother's milk 35 per cent. of total phosphorus is in the form of lecithin, while the lecithin of cow's milk is but 5 per cent. according to Stocklasa.[34]

The form in which the phosphorus reaches the organism is important for Salkowski has shown that the organism has not the power to build from phosphorus-free albumin, or from inorganic phosphates, cells which require as an integral part organically bound phosphorus.

Indeed, it has been shown that the phosphorus absorption is not in the least affected by the presence or absence of inorganic phosphates, but, on the other hand, the phosphorus absorption may be greatly increased when a child is fed on yolk of egg as shown by Cronheim and Muller.[35]

Phosphorus is in demand in the body, particularly in glandular structures and bones, and for the central nervous system, and we should expect to find a considerable daily need on the part of the growing organism. This need seems satisfied in the healthy breast-fed infant on an intake varying from 0.7 to 0.8 gm. as a minimum and 1 to 2 gm. as a maximum. This is a wide variation, but we should consider that phosphorus is one of the minerals which becomes a definite part of the tissue structures throughout the body, and by virtue of its close connection

33. Kellar, A.: Arch. f. Kinderh., xxix, Stuttgart, 1900, p. 1.
34. Stocklasa: Ebenda, 1897, xxiii.
35. Cronheim and Muller: Ztschr. f. diät. u. physik. Therap., 1903, vi.

with the albumin molecule must likewise suffer destruction along with the albumin, therefore it varies with the protein need.

The investigators who have determined phosphorus balances on infants are Blauberg, Michel, Keller, Cronheim and Muller and Schlossman. Let us consider some of their findings in comparison with the determinations which I have made.

ABSORPTION

It will first be noted that the intake of phosphorus is nearly ten times as great for cow's milk as for mother's milk and that in both forms of milk feeding the per cent. of intake absorbed indicates a very good absorption ability. In mother's milk, the absorption per cent. is 89.2 and that of cow's milk 53.2 in Blauberg's case. My determinations were 67.0 per cent., 78.1 per cent. and 83.0 per cent. on low, medium and high fat feeding. From this it would seem that phosphorus is more readily absorbed in the presence of increasing quantities of fat. The amount of the absorption depends more on the kind of phosphorus than on the quantity. The absorption of phosphorus is hindered when there is a relatively high ratio of accompanying alkaline earths and alkalies in the food; for example, when vegetables are fed a large calcium intake is present. This forms insoluble salts of phosphorus in the intestine and thus absorption is prevented. However, when these two elements meet within the body, they are joined in exceedingly close metabolic activity.

From my own determinations it appears that the phosphorus and nitrogen absorption varied considerably from the ratio in which these elements occurred in the food. Phosphorus absorption was relatively less than nitrogen absorption, during the low (2.1 per cent.) fat feeding, and was best in the medium fat feeding (4 per cent.), where it approximated the ratio which existed between nitrogen and phosphorus in the food.

RETENTION

The retention of phosphorus is one of great importance to the existence of life, for in conditions of starvation the organism clings tenaciously to its phosphorus—perhaps more so than to any other mineral constituent, except NaCl. This is probably due to its close connection with the central nervous system, for at the end of long periods of starvation the phosphorus content of nervous tissue is very little impoverished. This retention is, no doubt, in proportion to the need, and not only the present need, but it is stored up for an emergency; for the animal organism when fed on phosphorus-rich diet not only brings itself into phosphorus equilibrium, but retains a part of this excess phosphorus. The retention keeps step with the need and gradually diminishes when the skeleton is well formed.

As in the case of absorption, the phosphorus is retained not so much in proportion to its amount as according to the kind present. Its retention runs parallel with that of nitrogen in cases studied by Keller,[33] but L. F. Meyer[36] has been unable to confirm this finding, and in my determinations phosphorus and nitrogen were not retained in proportional amounts, i. e., 29.5 per cent. food-nitrogen was retained while only 4.8 per cent. of food-phosphorus was retained.

ELIMINATION

The elimination of phosphorus takes place both through the feces and through the urine. In most instances it is about equally divided between these two channels of excretion. However, great variations occur, for example, in children on a vegetable diet which contains much calcium, the phosphorus is largely excreted through the feces, since the calcium forms insoluble salts with the phosphorus and thus absorption is inhibited, while children on a generous flesh diet will excrete most of the phosphorus through the kidneys. The amount excreted through the urine on mother's milk varied from 0.04 to 0.08 gm., while on cow's milk it was much higher, being 0.589 gm. in Blauberg's case and as high as 2.009 gm. in one of my determinations. (See phosphorus tabulations.)

In the feces from mother's milk feedings, the elimination varied from 0.02 gm. to 0.036 gm., while on cow's milk it was 0.962 in Blauberg's case. My own determinations were 0.7648, 0.5991 and 0.3789 gm., the larger quantity appearing with the lower fat-content of feeding and diminishing as the fat was increased.

A number of investigators have tried to show that the elimination of phosphorus and nitrogen was parallel, arguing from the fact that with cell destruction both N and P were released; and, indeed, this is true for certain groups of tissues, and could we estimate their catabolism separately, this would be our result. However, since N is only influenced in the protein wear and tear of the body, and since phosphorus has many influences other than is brought about by its connection with nitrogen in the albuminous molecule, as a number of observers have shown—Ehrstrom, and more recently L. F. Meyer[36]—there may be nitrogen retention with a phosphorus loss, and vice versa. The fact, too, that phosphorus is retained so tenaciously, while nitrogen is more readily given up, is another reason why the ratio of $N:P_2O_5$ in the urine is of little value as an index to cellular metabolism. The phosphorus balance obtained by considering the intake and elimination through feces and urine can only be depended on for correct interpretation of metabolic activity of phosphorus, and, indeed, the same may be held for any of the food constituents.

36. Meyer, L. F.: Ztschr. f. physiol. Chem., 1904, xliii.

ANOMALIES IN PHOSPHORUS RETENTION

The anomalies related under the head of calcium retention are all shared in by phosphorus. Indeed, the pathologic conditions which affect one nearly always affect the other. As has been stated, in rachitis and osteomalacia there is a disturbance of retention of the phosphorus, particularly that part bound with calcium and magnesium. In these diseases the giving of calcium increases the retention of phosphorus and the giving of phosphorus increases the retention of calcium, proving undoubtedly their chemical and physiologic affinity.

Phosphorus has a close connection with intermediary metabolism, as shown by its large content in the thyroid gland, the ovaries and the testes. So great is the necessity for phosphorus in the functioning of the testes and ovaries that castration is sometimes employed in order to divert the phosphorus to the use of the bones, as has been done occasionally in osteomalacia.

In that anomaly known as phosphaturia, in which the ratio of P_2O_5 to CaO changes from 12:1 to 4:1, if a calcium-poor diet is given, the phosphates quickly disappear. Phosphorus may be retained in abnormally large quantities as pointed out by L. F. Meyer.[37]

SODIUM AND POTASSIUM

The relationship of potassium and sodium to the maintenance of the alkalinity is a very interesting and important one. The study of the influence of their *ions* on muscle-contractility and nervous irritability is yielding valuable data. The power of their *ions* to influence body weight, body temperature, pulse and even leukocyte count is a most important contribution made by L. F. Meyer[37] and S. Cohn.[23]

We will first discuss the problems of alkalinity into which Na and K enter, since these elements form the fixed alkalies. Under the anomalies of alkalinity we will discuss the problems which relate to variations of this alkalinity.

It should be remembered that both alkaline and acid solutions exist within the same body; that the blood, various secretions, as well as each body cell has a definite amount of alkali, and can vary only within very narrow limits in order that they may perform their proper functions. This automatic regulation of alkalinity of the tissues and fluids is one of the marvels of the human mechanism, and it is remarkable how rarely it varies sufficiently to produce a pathologic condition. It is for the maintenance of this stupendously important work that the fixed alkalies, sodium and potassium, are used. Albu and Neuberg[28] have explained this self-regulation thus: Through the tearing down of the albumin of the body and the albumin taken in in the food, sulphuric and phosphoric

37. Meyer, L. F.: Deutsch. med. Wchnschr., 1905, No. 37.

acids are set free and must be neutralized by the alkalies of the blood. These acids would draw out the fixed alkalies were it not for the supply of carbonate derived from the carbonic acid and from the vegetable salts taken in the food. At certain times when the breaking down of albumin is excessive, ammonia is also set free and this is used along with the carbonates for the fixing of the acids. By means of this sort of neutralization, the acids become a constituent of the body, the fixed alkalies remain untouched, and the alkalinity of the tissues is unchanged. Should this reaction suffer the least change, either through a lessening of the bases or an increase of the autogenous acids, the organism becomes at once in danger.

The constant chemical reaction is also necessary for the ferment action which takes place throughout the body. The alkalies act also as carriers of the carbonic acid in the blood-stream.

The *ions* of potassium and sodium have an important bearing on the heart action, as shown by Overton.[38] K *ions* do not seem an absolutely necessary accompaniment of rhythmical action, but if present in too large numbers they cause a depression, even to complete inhibition. On the other hand, Na *ions* are necessary to contractility and irritability of heart-muscle. If present alone they produce muscular relaxation.

Jacques Loeb[26] has shown how closely developing life is dependent on exact proportions of NaCl in solution as shown by his experiments in sea-water, physiologic salt solution and in water with no NaCl in it.

Let us, therefore, study the sources of supply of these important elements, and see if we can determine the daily need for the growing infant. (See tabulation on page 131.)

In mother's milk there is much less sodium and potassium than in cow's milk. There is more potassium than sodium in each of these milks. The daily need of the nursing infant as represented by the intake is for sodium 0.5877 gm., and for potassium 1.1032 gm. In cow's milk feeding the sodium intake was below the intake on mother's milk and the potassium intake was considerably above that on mother's milk.

ABSORPTION

The absorption is relatively good on both milks. On absorption the Na salt takes its place in the blood and tissue fluids, while the potassium, displaying its selective action, takes its place in the various body-cells and in the blood-cells. Its most common salts are potassium phosphate, which is the chief mineral constituent of red blood corpuscles, and potassium chlorid, which is found in the body-cells. The potassium salts make up 0.4 per cent. of the total blood and 0.65 to 0.8 per cent. of fresh muscle tissue. It is evident therefore that for the production of

38. Overton: Arch. f. d. ges. Physiol. Bonn (Pflüger), 1902, xcii, 346.

Potassium as K_2O

In 1,000 gm. mother's milk 0.69 gm. K_2O.
In 1,000 gm. cow's milk 1.885 gm. K_2O.

		——Elimination——		——Absorption——		——Retention——	
Food	Intake	Feces	Urine	Gm.	Per cent.	Gm.	Per cent.
Mother's milk (Klotz)	1.1032	0.2842	0.1591	....	....	0.6598	74.2
Cow's milk (Meyer)	1.9605	0.2033	1.4411	....	....	0.8161	16.12
Cow's milk (Blauberg)	1.57	0.271	1.12	1.30	82.8	0.180	11.5

Figures given above are in grams in 24 hours.

Sodium as Na_2O

In 1,000 gm. mother's milk there is .049 gm. Na_2O.
In 1,000 gm. cow's milk there is .465 gm. Na_2O.

		——Elimination——		——Absorption——		——Retention——	
Food	Intake	Feces	Urine	Gm.	Per cent.	Gm.	Per cent.
Mother's milk	0.5877	0.1924	0.1481	....	....	0.2471	67.2
Cow's milk	0.478	0.075	0.3305	....	....	0.0725	15.27
Cow's milk (Soldner)	0.409	0.098	0.343	.311	75.9	Negative	....

Figures given above are in grams in 24 hours.

the muscle of the growing child an adequate supply of potassium salts must be given.

RETENTION

The retention in per cent. of intake in mother's milk is very good, being 67.0 per cent. for sodium and 74 per cent. for potassium, while the retention on cow's milk is relatively poor, being 15.27 per cent. for sodium and 16.12 per cent. for potassium.

ELIMINATION

K and Na are eliminated through the urine and feces. The potassium in the urine is bound with Cl and with phosphorus and the sodium chiefly as NaCl. The sodium of the urine largely depends on the sodium intake in the food, while the potassium in the urine depends on the destruction of tissue; hence K metabolism is parallel with tissue destruction. This is explained by the fact that K is in the cells and is more closely bound, while Na is held in solution in the blood and tissue fluids and, therefore, more readily excreted. The normal ratio of Na to K in the urine is 3:1, 2:1 and some authors place it as 5:3.

ELIMINATION THROUGH THE FECES

About 15 to 25 per cent. of the intake of K and N are eliminated through the feces. These amounts vary considerably with the kind of diet, whether it is rich in alkali or not, or whether it is vegetable or made up of a considerable part of meat.

ANOMALIES OF RETENTION OF FIXED ALKALI

There is at times an over-retention of potassium salts to the point of potassium intoxication, and some authors[28] have attempted to build a theory for uremia on this fact. In such cases the potassium salts are retained in the blood-stream rather than taking their places in the tissue structure. But the most common anomaly is not that of over-retention but of marked withdrawal of the fixed alkalies. Against such a contingency the organism of the carnivora has builded up a strong resistance. First in the use of the carbonate of the tissue fluids and blood, and, as a last resort, in the production of ammonia. As has been previously stated, under normal conditions the carbonates with the help of a small amount of ammonia, are sufficient to care for the normal production of acids in the body. Under abnormal production of acids, as occurs in diabetes and in conditions of acidosis in certain infants fed on high fat mixtures, and in some older children fed on a mixed diet containing a quart or more of rich milk, there is a demand for a large quantity of ammonia to protect the fixed alkali.

A vast number of researches have been carried on covering the field of conditions of acidosis. It was Salkowski in his experiments on dogs

Chlorin as NaCl

In 1,000 gm. mother's milk, 0.294 gm. Cl.
In 1,000 gm. cow's milk, 0.82 gm. Cl.
In 1,000 gm. cow's milk (Hoobler), 1.8678 gm. NaCl.

		Elimination		Absorption			Retention		
Food	Intake	Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	0.3297	0.0135	0.1776	0.3162	95.4	....	0.1386	58.0	....
Diluted cow's milk, 2.1% fat (Hoobler)	2.3178	0.042	2.2421	2.2758	98.1	.274	0.0337	1.4	.004
Whole cow's milk, 4% fat (Hoobler)	2.3926	0.1567	2.3328	2.2359	93.4	.286	Negative	....	....
Cow's milk and cream, 5.4% fat (Hoobler)	2.3428	0.06031	2.1340	2.2824	97.3	.288	0.14849	6.3	.018

Figures given above are in grams in 24 hours.

who first pointed out that the self-produced body acids were bound by the withdrawal of the fixed bases of the body, and thus there would be impoverishment of these indispensable mineral constituents were it not for the fact that the carnivora are protected by this increased ammonia excretion; but this protection is only within narrow limits.

Not only is the withdrawal of alkali accomplished through the overproduction of acids, but it has been shown that a diet rich in fats will cause a withdrawal of alkali for the purpose of combining with the fatty acids of the stools. The fatty acids will first utilize such alkaline earths (Ca and Mg) as are available, and then for further neutralization will call on the fixed alkali of the body. This in turn demands the production of ammonia for the protection of the fixed alkali. This often occurs in healthy infants when on a high fat mixture, but it takes place preeminently, as shown by L. F. Meyer,[23] in the stage of decomposition of Finkelstein's *Ernährungstörung*. In this condition not only does the fat cause loss of alkali, but even sugar produces the same result.

SODIUM CHLORID

Of all the mineral constituents, sodium chlorid has the most varied and important functions to perform. The function of maintaining osmotic pressure has been the one most studied, and its relation to the retention and excretion of water is well known. In recent years to the Na *ions* and the Cl *ions*, acting either separately or in conjunction, have been assigned various results. L. F. Meyer[23] has shown that the intake of Na *ions*, especially when bound with the halogen group, particularly with chlorin, when in certain concentration, viz., 3 gm. NaCl to 100 c.c. water, always produced an increase of temperature in a young infant. There is a marked decrease in the body weight when fed on milk freed of salts; also the pulse and leukocyte count are affected. Just what the daily need of this salt is depends largely on the kind of food ingested. There is a certain demand for this salt and when the intake is cut off the body retains with great tenacity what it has until further intake occurs.

The chlorin intake in mother's milk is 0.3297 gm., while on cow's milk the chlorin intake in terms of NaCl was 2.3926. The tabulation on page 133 shows the chlorin metabolism in terms of NaCl.

The demand for NaCl is greater in herbivora than in carnivora, because of the greater consumption of K carbonates, as was pointed out in the classic observation by Bunge.[39] His concise explanation of this phenomenon is that with a large intake of K carbonate there is formed in the blood the salts of sodium phosphate and potassium chlorid. Both being foreign, they are eliminated, leaving a loss of NaCl which must be replenished.

---

39. Bunge: Cited by Albu and Neuberg, Mineralstoffwechsel, p. 164.

NaCl is ingested in large quantities. It being well absorbed, there is an increased quantity in the blood, hence its isotonicity is disturbed and either there must be a holding back of water until the solution is isotonic, or an increased elimination of the NaCl. Both of these processes may take place.

ABSORPTION

The absorption of salt is found to be excellent—usually above 90 per cent. of the intake is absorbed. The retention of NaCl is only sufficient to cause a balance to be maintained under normal conditions. In my determinations I found that there was utilized but 1.4 per cent. to 6.3 per cent. of the intake.

ELIMINATION

The elimination takes place almost entirely through the kidneys. But a very small quantity appears in the feces, so well is it absorbed. In my determinations there was a little over 2 gm. excreted through the urine daily, while less than 0.1 gm. appeared in the feces.

It has been observed that salt solution when injected subcutaneously is more quickly eliminated than when taken by mouth. With the excretion of NaCl there must accompany it a certain amount of water, and, therefore, the intensity of diuresis depends on the molecular concentration within the body. Not only does salt affect the retention and withdrawal of water, but it holds a very close relation to nitrogen.

Voit's original work seemed to show that with increasing retention of NaCl there was an increased retention of nitrogen; later investigations have not agreed with this. Belli[40] sums up his findings with the statement that in small amounts, as in the food normally, it hastens and increases protein retention, but in greater quantities it tends to lessen the nitrogen retention.

THE ANOMALIES OF NaCl RETENTION

There are a number of conditions which seem markedly affected by sodium chlorid. The most important is that of nephritis. Von Noorden[41] was the first to work on this important condition. He noted a variation in different cases. Some retained and others did not retain NaCl. Halpern[42] has shown that both in acute and chronic nephritis the salt content of the urine is dependent on the salt content of the food. In cases in which there is edema there is marked lessening of the edema when the patient is put on a salt-free diet, and there appears in the urine an increase in the NaCl elimination. The use of salt-free diet, whether

40. Belli: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 170.

41. Von Noorden: Lehrbuch d. Pathologie d. Stoffwechsels, Berlin, 1893.

42. Halpern: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 174.

with or without edema, brings about more or less of a dechloruration of the body. It would seem that in these cases the NaCl retention always precedes the water retention and that the edema consequent on water retention is due to the NaCl retained. However, no hard and fast rules can be laid down in regard to use of salt-free diet, as in some cases it will not reduce edema, and in some cases a salt-rich diet will not always produce NaCl retention.

L. F. Meyer[23] believes that many of the symptoms present in food disturbances of infants may be traced to the deleterious influence of sodium chlorid, acting not only as salt, but also in the capacity of the respective *ions*. He believes particularly that the rises of temperature during the stage of intoxication of Finkelstein's *Ernährungstörung* is due to the action of these *ions*. In children with food disturbances smaller quantities of NaCl solution will raise temperature more quickly than in healthy children.

Fisher[43] has shown that the injection of salt solution of one-sixth molecular strength may produce glycosuria, and that this glycosuria may be stopped by injecting a calcium chlorid solution.

Abderhalden[6] believes that every cell has particular salts in specific apportionment and that a disturbance of this relation, as would take place in Fisher's experiment just quoted, would cause considerable trouble in the life processes of the cell.

SULPHUR

Of all the mineral salts, sulphur has been the last to receive due attention at the hands of investigators. What we know of sulphur metabolism is largely due to Freund[46] and his pupils. Sulphur presents itself for ingestion in the food in two different forms, viz., in the inorganic salts, and organically bound with albumin. The inorganic salts have little or no effect on metabolism and need not be considered. It is that sulphur which is organically bound which is the important part and which supplies the daily need of the growing infant.

Whether or not sulphur is necessary for the maintenance of life is still a question, but any substance so closely associated with nitrogen may be assumed to have a distinct function, though as yet this function is obscure.

The total sulphur intake of infants fed on mother's milk is .04 gm., while on cow's milk the daily intake is about 0.44 gm., according to my recent researches. The sulphur of mother's milk is very well absorbed, as is also that of cow's milk. My determinations show that it is absorbed in from 88.2 to 95.7 per cent. of intake. This absorption is quite in

43. Fisher: Cited by Abderhalden, Lehrbuch d. physiolog. Chemie, Berlin, 1909, p. 358.

46. Freund: Zeit. f. phys. Chem., Strassburg, 1900, xxix, 24-46.

Sulphur in Terms of S

In 1,000 gm. mother's milk, total sulphur .0572 gm.
In 1,000 gm. cow's milk (Hoobler), total sulphur .33538 gm.

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	.0396	.0096	.026	.0298	75.5	....	.0039	9.8	....
Cow's milk	.5832	.01484	.2019	.0436	74.5	....	Negative	....	....
Diluted cow's milk, 2.1% fat (Hoobler)	.46308	.0542	.3777	.4089	88.2	.491	Negative	....	....
Whole cow's milk, 4% fat (Hoobler)	.4411	.02430	.26589	.4168	94.2	.531	.15091	34.2	.019
Cow's milk and cream, 5.4% fat (Hoobler)	.4444	.01901	.30585	.42546	95.7	.533	.11961	26.9	.015

Figures given above are in grams in 24 hours.

keeping with the facility with which nitrogen is absorbed, and this is probably due to the fact that its connection with the albumin molecule is so close. (See tabulation, page 137.)

The absorption takes place through the small intestine, and some of it is again eliminated into the large intestine, making up the sulphur found in the feces.

Schwarz[47] found in a 5-year-old child on a mixed diet that the absorption was very good, being 92.2 per cent. of the intake. My normal child on a milk diet had an absorption of 92.4 per cent. of the intake. Identical methods of determination were used by both of us.

RETENTION

The retention of sulphur in mother's milk feeding is very good, while with cow's milk the retention is relatively poor. In one of my determinations there was a negative balance and in two others 34.2 and 26.9 per cent. of the intake was retained. Schwarz,[47] in a normal 5-year-old child on a mixed diet found that sulphur retention was relatively poor, being 31.1 per cent. of the intake.

ELIMINATION

The elimination of sulphur occurs mostly through the urine. In cow's milk feeding ten times as much appeared excreted through the urine as through the feces.

The sulphur in the feces appears as iron sulphate and alkali sulphate, while in the urine there are recognized four different forms, viz., the inorganic sulphate sulphur, the ethereal sulphate sulphur, neutral sulphur and basic sulphur. The first named is by far the most abundant in the urine, making up about 80 per cent. of the total sulphur. Ethereal sulphate sulphur makes up about 8 per cent. of the total sulphur and the neutral and basic sulphurs the balance.

Just what significance should be assigned to total sulphur and to each of the various sulphurs making up the total, has been the subject of much speculation.

Because of the connection between sulphur and albumin in tissues, the sulphur metabolism has been taken as the index to protein metabolism. The normal ratio is $N : H_2SO_4 : : 5 : 1$.

The relative amount of ethereal sulphate sulphur has been taken as an index of the degree of albuminous putrefaction going on in the intestine, and also for the breaking down of albuminous cells in the body.

The neutral sulphur appears to be increased on a vegetable diet and decreased on a meat diet. Investigators have shown that in periods of starvation, as well as in other conditions of protein break-down, there is an increase in the per cent. which neutral sulphur holds to total sulphur.

47. Schwarz: Jahrb. f. Kinderh., 1910, lxxii, p. 549.

Lepine[48] is the authority for believing that neutral sulphur has its origin partly from the taurin of the bile. This is first excreted into the intestine, reabsorbed, and again eliminated through the urine. In those conditions of disturbed oxidation, if below normal, neutral sulphur is low; if above normal, then the neutral sulphur is increased. In my determinations of neutral sulphur it appears that on cow's milk containing 2.1 per cent. fat the neutral sulphur averaged 7.2 per cent. of the total sulphur, but that on feeding 4 per cent. and 5.4 per cent. fat mixtures the neutral sulphur was increased to as high as 15 per cent., more than doubled. This might be explained by the fact that during these higher fat feedings small amounts of acetone, diacetic acid and beta-oxybutyric acid were found in the urine, forecasting an impending acidosis, in which already tissue albumin had begun to disintegrate.

ANOMALIES OF SULPHUR RETENTION

Schwarz has shown that in rachitis the total sulphur absorption in two cases was 76.9 and 83 per cent., which was somewhat lower than in his normal case, which showed 92.2 per cent. absorption. The retention in one case was 30.9 per cent. and in the other 26.1 per cent. of the intake. This was about the same as in his normal case, viz., 31.1 per cent.

There was eliminated through the urine 55 per cent. of the total sulphur in one case and 54.1 in the other, while in the urine of his normal case 61.1 per cent. was thus eliminated. The elimination by the feces in two of his cases of rachitis showed a marked change from his normal case—23.1 per cent. and 17 per cent. in rachitis and but 7.8 per cent. in the normal.

Of the various forms of sulphur in the urine, the only one which showed much variation from the normal was that of the neutral sulphur, which in two of his cases was considerably increased, being 18.5 per cent. and 18.6 per cent., while his normal showed 7.8 per cent. of the total sulphur. In one of his rachitic cases no variation from the normal occurred.

A further anomaly of sulphur metabolism is that of cystinuria. Bunge has shown that in the catabolism of cystin, albumin, which has sulphur in it, sets sulphur free, which usually unites with bases and is eliminated as sulphates; but if the bases are lacking, then alkali is drawn from the cells of the body.

SUMMARY

1. Salts are necessary to maintain life.

2. Salts are best absorbed and utilized when in organic combination with food stuffs.

48. Lepine: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 148.

3. There are marked differences in the salt content of mother's and cow's milk which should be considered in artificial feeding.

4. Certain pathologic conditions arise in which certain of the salts are not absorbed, even though in abundance in the food.

5. In certain other pathologic conditions salts are actually withdrawn from the body to such an extent as to impoverish the organism and produce grave disturbances of nutrition.

6. The various salts, with the exception of iron, are present in sufficient quantities and proper proportions in mother's milk. In most of the dilutions of cow's milk there is an excess of salts which may be neglected in feeding normal infants, but which plays an important rôle in the feeding of children already suffering from nutritional disturbances. The conditions under which the salt content of feedings should be altered and in just what degree each or all should be varied, are still unsolved problems.

131 East Sixty-Seventh Street.

PROGRESS IN PEDIATRICS

ACUTE INFECTIOUS DISEASES

Poliomyelitis

The unfailing regularity with which the United States has been visited by epidemic poliomyelitis makes it insistent that every practitioner in the country should be conversant with the progress of knowledge in regard to this malady.

In the past four years it has become widely distributed. Its ravages have extended completely across the continent; but few of the Southern States, even, having been free from the scourge.

Before 1907 the most clearly defined focus of the disease was in Scandinavia, and the first point affected by poliomyelitis in this country was the part of the Middle West in which a large settlement of Scandinavians had formed.

According to the information procured during the Scandinavian epidemics, it would appear that the contagion can be carried from the ill to the well by intermediate agencies. The incubation period is variable, but the mean is about ten days in length—a space of time equal to that required for the journey from affected districts in Europe to the United States.

These, and certain other equally suggestive circumstances, have led to a widespread renewal of interest in the epidemiology of the disease.

Experiment, and the observation of large numbers of cases, have of late helped us vastly to an accurate conception of processes which only a few years ago were subjects of the vaguest surmise. Unfortunately we cannot as yet point definitely to any precise method of prevention; nor yet even to a method whereby the severity of an epidemic already existing may be diminished; nor yet, again, are we in a position to be able unfailingly to abort the progress of these pathologic conditions in individual cases. However, the sum of knowledge has in the past three years been enormously augmented, and it must be a source of satisfaction to every American that the credit for these advances is mainly due to workers in American hospitals and laboratories.

An attempt will now be made to sketch as briefly as may be an outline of the more important of these results.

In the summer of 1909 Landsteiner and Popper succeeded in producing the disease in two monkeys by intraperitoneal injection of the emulsified spinal cord obtained from a fatal case of poliomyelitis. They failed, however, to transmit the disease from these to other monkeys.

In September of the same year Lewis and Flexner in this country also succeeded in producing the disease in monkeys by means of intracerebral injection of poliomyelitic cord. The cords of the affected monkeys furnished a virus to these observers which, by September, 1910, they had propagated through twenty-five separate series of monkeys.

The incubation period was taken to be the length of time between the date of inoculation and the first appearance of definite paralysis; this was of variable length, but the average corresponded to the ten days already surmised to be the incubation period in human poliomyelitis. In the early part of this period the animals showed no sign of ill-health, but from six to forty-eight hours before the onset of paralysis they became nervous and excitable, and easily tired. Their gaze became shifting rather than fixed, as it is in the normal animal. The temperature was not much raised and gastro-intestinal symptoms were infrequent.

These somewhat vague prodromal signs were followed by the onset of paralysis, the distribution of which corresponded almost precisely with that found when the disease occurs spontaneously in man.

The inoculated disease in monkeys differs markedly in its mortality from the human affection. At least half of the animals inoculated died, whereas the fatal cases in human poliomyelitis do not exceed 10 per cent. of those attacked even in the most severe epidemics. But it might here be suggested that the notorious delicacy of the monkey, especially in captivity, is sufficient completely to remove this single discrepancy between the human and experimental conditions.

The lesions produced in the central nervous system in both the spontaneous and experimental diseases are almost exactly similar.

The microscopic lesions in the brains and cords of monkeys dying of the disease consisted mainly of congestion and hemorrhages into the gray matter; the anterior horns being disproportionately affected. The entire spinal cord was involved in a series of wide-spread vascular accidents, the cord injury, however, corresponding in position to the greater palsies of muscle groups.

The lesions consisted of a small round-celled infiltration in the perivascular spaces with the development of considerable edema. Arterial thrombosis was never apparent, and the degeneration and necrosis of cells was invariably produced by gross pressure of inflammatory exudates on the cells and the nutrient blood-vessels. A leptomeningeal infiltration of mononuclear cells was always present and was perivascular in position.

The greater affection of the anterior over the posterior horns is explicable by the richness of the vascular supply to the former; a similar consideration serves to explain the apparently disproportionate involvement of the lumbar and cervical enlargements.

The organism of poliomyelitis belongs to the class of filtrable viruses; its potency is not reduced by being passed through a Chamberland filter. The clear fluid obtained by filtration of poliomyelitic cords has been seen to contain innumerable bright, dancing spots when examined under the dark field microscope; these points were not found in filtrates similarly obtained from normal cords; it remains to be seen whether or not they represent the organism of the disease.

It is doubtful if the virus can be grown in culture media. It withstands glycerinization, drying, and freezing over prolonged periods, but is readily destroyed by heat, and by comparatively weak antiseptics, such as menthol, and a 1 per cent. solution of hydrogen peroxid.

The virus is contained in the brain, spinal cord, lymphatic glands, salivary glands and nasal mucosa. At the beginning of the infection the blood and cerebrospinal fluid have also been found, sometimes, to be capable of producing the disease when injected into a suitable host.

It can be inoculated with success into the brain; into the subdural space; subcutaneously. Infection has been produced by the introduction of toxic filtrate into the stomach by means of a catheter, and by injection into the intestines; a necessary condition, however, being the previous exhibition of opium to restrain peristalsis. The disease has also been caused by rubbing the nasal mucous membranes with a toxic suspension, though for certain success, previous scarification of the nasal mucosa is required. A similar proviso applies to infection *via* the trachea and the rest of the respiratory tract.

Attempts to inoculate the disease in monkeys which had been already attacked were invariably unsuccessful. Further, the serum of both monkeys and human beings recently recovered has been found to possess the power of diminishing, or occasionally completely neutralizing the virus *in vitro*, and in the bodies of infected monkeys.

If hexamethylenamin (urotropin) be administered to a monkey, it is excreted into the cerebrospinal fluid. If, then, that monkey be inoculated, the incubation period will be frequently prolonged, and the severity of the attack diminished. Further, if in addition to the administration of hexamethylenamin, the animal be injected with immune monkey-serum, the onset of paralysis is most often entirely prevented.

Kraus has recently shown that the injection of 10 c.c. of poliomyelitis virus, sterilized by being treated with 1.5 per cent. phenol, completely protects the macacus against subsequent inoculation of active virus, an observation which, if confirmed for man, opens up the possibility of successful vaccination against this disease.

The active immunity conferred by an attack of poliomyelitis obtains, apparently, for a period of at least three years. Active immunization of monkeys has been achieved by the repeated inoculation of small doses of virus over a period of several months, after which an inoculation of maximum potency was harmless. Previous glycerinization of the virus apparently renders it more suitable for immunizing purposes.

In the attempt to obtain an artificial antiserum it has been found that the normal sheep-serum has the power definitely to diminish the potency of the filtered virus; and if the sheep be previously injected with immune monkey-serum this neutralizing property becomes markedly augmented.

It must, however, be pointed out that the endeavor to produce an entirely satisfactory antiserum has not as yet met with success; that much experimentation must still be completed; and that the ideal antiserum, when obtained, will have to be employed in the very beginning of the disease before any lesion of the central nervous system has yet occurred—a condition which makes it necessary for us to achieve more exact methods of diagnosis in the prodromal period of the condition.

The symptomatology of the disease is so well known that it seems almost unnecessary to dwell long on this section of the subject.

The eight classes to which Wickman drew attention may be mentioned:

1. Spinal poliomyelitis form—a sudden feverish attack followed by the palsy of one or more limbs.

2. An ascending form in which, first, are involved the legs, and later the muscles of the abdomen and thorax. This type is often fatal.

3. A bulbar type, with palsies of the various pontine and medullary cranial nerve nuclei.

4. Polio-encephalitis, from which a state of meningismus with spastic paralyses may ensue. Koplik, in a notable paper in the *American Journal of Medical Sciences* has done much clearly to depict the clinical picture presented by this condition.

5. Ataxic polio-encephalitis, by which is merely meant an inflammatory process, the maximum stress of which falls on the cerebellum. The clinical symptoms are briefly, an acute illness of short duration, followed by motor ataxia of the arms and legs, nystagmus and explosive syllabic speech. The writer has not been able to find statistics on the frequency of occurrence of this form of the disease, but his impression has been that it occurs in adults more frequently than do other types of the affection.

6. The polyneuritic form; practically impossible to diagnose as a distinct entity, but its existence has been proved by autopsy.

7. The meningitic form. Since Wickman's formulation our knowledge has been advanced sufficiently to show us that practically in all cases the meninges are very markedly affected. Clinical and pathologic studies combine to make it needless to classify separately this condition.

8. Abortive forms in which only general constitutional disturbances occur, and paralyses are either quite fleeting, or entirely absent. The correct diagnosis in these cases can only be surmised from the co-existence of an epidemic of the disease, though possibly assistance may be obtained from the picture presented by the blood and cerebrospinal fluid.

Experimental studies by Flexner and Lewis show that in the preparalytic stages the cerebrospinal fluid exhibits definite evidences of the round-celled infiltration of the meninges to which references have already been made. Within forty-eight hours of inoculation the fluid is found to be under increased pressure;

a little later it contains an increased number of lymphocytes which give it an opalescent appearance; its coagulability is also greatly increased. These changes have disappeared by the time definite palsies have developed.

These facts, coupled with Muller's observations, confirmed by many observers, that in the initial febrile period there are leukopenia, profuse sweating and intense hyperesthesia, give us some hope, but no certainty, of being able to recognize the early stages of the disease by the time the laboratory workers put weapons into our hands.

The fact that the mucous membrane and salivary glands of infected monkeys have been shown to be potent to reproduce the disease, would appear to justify us in supposing the secretions of these to be infective; the cribriform plate offers the most convenient avenue for the passage of organisms between the meninges and the external world, a consideration which must be borne in mind when we come to draw up preventive measures.

It is certain that the period in which epidemic poliomyelitis is most violent includes the warm, dry months of August and September; it is not clear that density of population is any factor in the proportionate severity of any particular epidemic, and the problem of the method by which the disease frequently is transmitted in little populated and extensive districts, is one difficult of solution.

A notable contribution to the clearing up of this question was lately made by workers in the Rockefeller Institute, who succeeded in producing the disease in monkeys by the intracerebral injection of an emulsion, made from the bodies of common house-flies, which had been fed on portions of spinal cord obtained from a poliomyelitic monkey.

The direct contagiousness of poliomyelitis is exceedingly slight; true, many times two or three cases have occurred in one family, but the transmission of the disease from one patient to another has been difficult of proof, and the sporadic and apparently well-isolated cases far out-number those in which infection could be argued for with any conviction; the spread of an epidemic seems to be independent, too, of poisoned food or water-supply, though the general direction is usually along low-lying parts of the country, and especially along those in which water areas exist.

The trend of all these considerations would seem to indicate the transmission of the disease, not by contact or infection as in measles or scarlet fever, not by ingestion of toxic material, but rather by the intermediate agency of insects; for detail in this theory—or for its condemnation—further experiment must be awaited.

All authorities demand strongly, however, that the disease be made universally reportable, and it is to be hoped that legislation to this effect will speedily be achieved.

In view of our yet nebulous knowledge as to the transmissibility and contagiousness of the condition, all cases should be isolated, and it would be well to insist that the same precautions be observed as would be applicable in a case of scarlet fever.

In addition to these precautions, particular care should be taken to disinfect the nasal and pharyngeal passages by means of the frequent use of a spray of 1 per cent. solution of hydrogen peroxid. In February of the present year it was proved that the nasal mucous membrane may remain infective for some five or six months, so it would appear that this antiseptic treatment should be extended for a time considerably longer than the duration of acute symptoms.

As a prophylactic measure the routine use of hydrogen peroxid on the part of those living in the neighborhood of infection should be encouraged.

The results of insect experimentation indicate the necessity of the inauguration of a campaign against the common house-fly. Perhaps it is not too much to suggest that united action against this pest might result in beneficial effects to the public health in more directions than that with which this paper more particularly deals.

FOSTER KENNEDY.

NOTICE

Circular issued by the American Orthopedic Association and the American Pediatric Society in reference to acute epidemic poliomyelitis, addressed to health authorities and boards of health.

Anterior poliomyelitis is, so far as known, a communicable disease, being communicated from one patient to another and also by means of a third person. It occurs in epidemics and tends to spread along the lines of greatest travel. There is reason to believe that it is prevented from spreading by quarantine, and with the very great prevalence of the disease in the summer of 1910 it is the opinion of this committee that it is essential that it should be made a reportable disease in all states in order that its presence may be detected and its spread guarded against.

Of particular significance are the so-called abortive cases, in which indefinite ailments occur in children in communities where frank paralysis also exists. These abortive cases of infantile paralysis are undoubtedly a source of infection, and their record and study is of much importance. In a community where cases of infantile paralysis occur, cases of illness with sudden onset of fever and meningeal symptoms should be closely watched and regarded as possibly infectious. In such cases even recovery without paralysis does not establish the fact that the case was not abortive infantile paralysis.

All cases of infantile paralysis should be strictly quarantined, sputum, urine and feces being disinfected, and the same rigid precautions should be adopted as in scarlet fever. This quarantine should, in the opinion of the committee, last for four weeks, in the absence of definite knowledge as to when the infection ends. Children from infected families should not be allowed to go to school until the quarantine is abandoned. The transportation or transfer of acute cases in public conveyances should be strictly forbidden. It would be very desirable to adopt provisional quarantine measures in suspicious cases in a community in which an epidemic prevails.

The report of all cases of infantile paralysis to the public health authorities should be enforced by law, and all deaths from this cause should be properly described and registered. A careful study of epidemics by public health authorities is strongly advised.

ROBERT W. LOVETT, M.D., Chairman.
HENRY KOPLIK, M.D.
H. WINNETT ORR, M.D.
IRVING M. SNOW, M.D., Secretary.

The Rockefeller Institute for Medical Research of New York City announces that it will devote its resources very largely during the present season to the study of anterior poliomyelitis (infantile paralysis) and to the treatment of acute cases of this disease in its hospital. Physicians and health officers desiring to co-operate in this investigation may do so by sending information concerning the occurrence and prevalence of this disease, or by referring acute cases to the Hospital of the Rockefeller Institute. Dr. Flexner renews his request of last year that whenever possible a portion of the spinal cord and of the nasopharyngeal mucosa derived from fatal cases of the disease be sent to him. Specimens should be preserved in glycerin and sent by mail to Simon Flexner, M.D., Sixty-Sixth Street and Avenue A, New York City.

The Occurrence of Infantile Paralysis in Massachusetts in 1910

(*R. W. Lovett, P. A. E. Sheppard: Boston Med. and Surg. Jour., 1911, clxiv,* 737)

Three classes of cases are reported on. 1. The total number reported by physicians—845. 2. The number for which blanks were filled out—601. 3. A

group carefully studied by investigators of the board—200. A study of the rainfall for the last ten years shows that during the last four years, when the disease has been carefully studied the driest years have not been attended by the largest number of cases. In 1910 the month with the least rainfall and the highest mean temperature (August) also had the largest number of cases. An investigation of the nearness of the affected houses to railroad or highroad or to water showed no predominating number close to any. Nothing could be found in the age of the house, its sanitary condition, the water-supply, or sewage disposal which might be assigned as a possible cause. Measurement of the amount of dust is inaccurate, but 316 out of 601 streets are reported as having "no treatment." Study of the prevalence of insects must be made on the spot by a person skilled in entomology. Thirty-four homes out of 110 had illness, paralysis or death in eighty-two animals near the time of the human paralysis. The apparent partial immunity of the colored race may be less true than has been supposed. In Springfield there was in incidence of 3.09 per 1,000 among the colored and 1.99 per 1,000 among the white population. In 200 cases carefully studied there was certain direct contact with acute cases in thirty-two cases, indirect contact in ten and direct contact with a possible abortive case in four. Investigations concerning the diet were not of especial interest. Just previous or some time before the attack 60 per cent. of patients had some abnormal condition—malaise, gastro-intestinal or respiratory disturbances. Study of recent illnesses in the same family showed nothing of importance. During the attack 75 per cent. showed some digestive disturbance. Pain and tenderness occurred in 469 out of 601 cases, lasting most commonly one to three weeks. The paralysis nearly always developed within one week after the onset of fever. The back, abdomen, neck and face are frequently involved. Out of 200 patients, 13.5 per cent had entirely recovered at the end of six months. RICHARD M. SMITH.

METABOLISM AND NUTRITION

Determination of Casein in the Curd of Infant Stools by Biologic Methods, Especially Anaphylaxis

(*A. Uffenheimer and Y. Takeno: Ztschr. f. Kinderh., ii, No. 1, p. 32*)

It is held by the authors that when the present day pediatrician speaks of casein curds he refers to something which really does not contain casein. The curds to which they refer in their article are those which are found frequently in the feces of nurslings and which vary in size between that of a pinhead and a pea. They are not the same bodies of which Selter and Talbot have written. These, it is held, possess certain peculiarities and are also found in the stools of children suffering from some digestive disturbance. The present paper details the work done with a view to determining the composition and nature of these curds. First they attempted to use the precipitation method of Hamburger and Knoepfelmacher by means of cow-lactoserum. However, it did not prove practicable and therefore the anaphylactic method was resorted to. The guinea-pig was used and horse serum was injected. The curds were obtained from a large number of diapers, irrespective of the particular sort of food which the children had been taking; in fact, the authors had no knowledge on the subject whatever. Guinea-pigs were injected with the material obtained, some of them intravenously and others subcutaneously. Curds were obtained from twenty-four children. Twenty-two of these were fed on various dilutions of cow's milk. In the case of nine of these the presence of casein was determined by the anaphylactic method twenty-six times. In the case of three children fed on mother's milk, the result was always negative. It was specially interesting that in the case of one infant on whom five examinations were made during the time he was fed

on cow's milk, casein was invariably found present in the curd. The positive findings obtained when the curds were treated with a decinormal caustic soda solution convinced the authors that the casein was not denatured. They injected small quantities of a caustic soda casein solution and then followed with an injection of 4 c.c. of a diluted milk solution. In one case severe shock occurred and death in three minutes; in another, extreme emphysema, rapid heart beat, etc.; and in another, severe general disturbances with temperature reduction to 33.2 C. In the next experiments the authors first injected the diluted milk solution and then the curd mixture. The sensibilatrice was the caustic soda casein or the diluted milk solution and the anaphylactic test was made with the curds which it was previously determined contained casein. Four out of five of the experiments were positive. Twenty-one precipitation tests were made with dilutions of lactoserum varying from 1 to 100 and from 1 to 1,000. The result was a negative one in every instance except two. These two examinations were made of the stool of the same child and in each case there was a slight precipitation. Subsequently, forty-four further examinations were made with a better lactoserum than was used in the first instance, the dilution being 1 to 3,000. Of the fourteen children examined seventeen positive results were obtained in five of them. The authors believe that both methods have given the same results, although they prefer the anaphylactic method because of its greater accuracy. They believe that their experiments prove conclusively that the curds found in the stools of sick nurslings fed on cow's milk very often contain casein. They raise the question, however, whether this casein is unchanged casein or para-casein, and they ask again if this substance reacts in the same manner as native casein. F. C. Z.

Nutrition and Growth

(*Hans Aron, Philippine Jour. of Sc., 1911, vi, 1*)

The relationship between nutrition and growth was made the subject of a very exhaustive experimental study by Aron. He made four sets of experiments on fourteen dogs, and noted (1) the influence of a restricted diet on growing dogs; (2) effect on the weight and appearance of the animals; (3) relative amount of change in certain parts of the body as compared with other parts; (4) changes in the chemical constitution of the body; (5) energy requirement and food consumption. Then he studied (1) the biologic considerations concerning the suppression of growth by restricting the food; (2) energy required during growth, and (3) the increase in weight as an index to growth, with special reference to children. The most important results of his experiments may be summarized as follows: A growing animal which receives only sufficient food to keep its body weight constant, or to allow a slight increase, is in a condition of severe starvation. If by a restriction of food the increase in weight is inhibited, the skeleton grows at the expense of other parts of the body, especially of the flesh. Most of the organs retain their weight and size, while the brain grows to reach its normal weight. The composition of the body, when at a constant weight, undergoes remarkable changes: Fat is consumed more or less entirely, the quantity of protein, especially of the muscles, but not of the organs, is diminished and a great proportion of the body tissues is replaced by water; thus, this water and the increase of the skeleton together, replace the body materials lost. The caloric value of 1 gm. body weight of an animal which has undergone such a process to its extreme limit may amount to only one-third of the normal value. It is possible by supplying suitable amounts of food to maintain a dog in an emaciated condition, apparently in good health, and at the weight of a puppy, for nearly one year, while its weight at the end of the

year should be three times as great. If such an animal is thereupon fed amply, it fattens and rounds out, but does not reach the size of a control animal which from the beginning has been normally fed. It is unable to make good the growth suspended by the long restriction of food. The growth principally depends on the tendency to grow possessed by the skeleton. The skeleton loses its capability of growing in more advanced age regardless of the size which the animal has reached. F. C. Z.